Hidden shift of the ionome of plants exposed to elevated CO_2 depletes minerals at the base of human nutrition

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Abstract Mineral malnutrition stemming from undiversified plant-based diets is a top global challenge. In C_3 plants (e.g., rice, wheat), elevated concentrations of atmospheric carbon dioxide (eCO_2) reduce protein and nitrogen concentrations, and can increase the total non-structural carbohydrates (TNC; mainly starch, sugars). However, contradictory findings have obscured the effect of eCO_2 on the ionome—the mineral and trace-element composition—of plants. Consequently, CO_2-induced shifts in plant quality have been ignored in the estimation of the impact of global change on humans. This study shows that eCO_2 reduces the overall mineral concentrations (−8%, 95% confidence interval: −9.1 to −6.9, $p<0.00001$) and increases TNC:minerals > carbon:minerals in C_3 plants. The meta-analysis of 7761 observations, including 2264 observations at state of the art FACE centers, covers 130 species/cultivars. The attained statistical power reveals that the shift is systemic and global. Its potential to exacerbate the prevalence of 'hidden hunger' and obesity is discussed.
DOI: 10.7554/eLife.02245.001

Introduction

Mankind's ultimate source of carbohydrates is atmospheric carbon dioxide (CO_2) converted by photosynthesis to sugars. The bulk of the terrestrial conversion of CO_2-to-carbohydrates is done by C_3 plants, which account for over three quarters of global primary production and for over 90% of Earth's plant species (*Still and Berry, 2003*). (*If not stated otherwise, hereafter, terms 'plant(s)' and 'crop(s)' refer to C_3 species*). When exposed to CO_2 concentrations twice the preindustrial level of ~280 ppm, plants increase the synthesis of carbohydrates by 19–46% (*Leakey et al., 2009*). Currently, CO_2 concentrations are reaching 400 ppm—the highest level since the dawn of agriculture and likely to be the highest since the rise of modern humans (*Siegenthaler et al., 2005*). Within a single human lifespan, CO_2 levels are projected to reach 421–936 ppm (*IPCC, 2013*). Will rising CO_2 concentrations—one of the most certain and pervasive aspects of global climate change—alter the quality of crops and wild plants? Will the CO_2-induced stimulation of carbohydrate synthesis increase the carbohydrates-to-minerals ratio in crops? Can such shifts in crop quality affect human nutrition and health?

Elevated CO_2 effects on plant *quantity* (productivity and total biomass) have been extensively studied and show higher agricultural yields for crops, including wheat, rice, barley, and potato. But eCO_2 effects on plant *quality*, and possible cascading effects on human nutrition, have been largely ignored in the estimation of the impact of eCO_2 on humans. Notably, *IPCC (2007, 2013)* and *AAAC Climate Science Panel (2014)* include direct CO_2 effects (e.g., ocean acidification) in their climate change assessments but do not mention any CO_2 effects on crop or wild plant quality. However, it is unwarranted to assume that plants will balance the increased carbohydrate synthesis with other adjustments to their physiology to maintain the nutritional quality for their consumers in a state of unperturbed homeostasis. The stoichiometry—the relative ratios of chemical elements—in plants is plastic and, to a considerable degree, reflects their environment (*Sterner and Elser, 2002*). However, detecting CO_2-induced shifts in plant quality is challenging for several reasons. First, plant quality involves

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eLife digest Rice and wheat provide two out every five calories that humans consume. Like other plants, crop plants convert carbon dioxide (or CO_2) from the air into sugars and other carbohydrates. They also take up minerals and other nutrients from the soil.

The increase in CO_2 in the atmosphere that has happened since the Industrial Revolution is thought to have increased the production of sugars and other carbohydrates in plants by up to 46%. CO_2 levels are expected to rise even further in the coming decades; and higher levels of CO_2 are known to lead to lower levels of proteins in plants. But less is known about the effects of CO_2 levels on the concentrations of minerals and other nutrients in plants.

Loladze has investigated the effect of rising CO_2 levels on the nutrient levels in food plants by analyzing data on 130 varieties of plants: his dataset includes the results of 7761 observations made over the last 30 years, by researchers around the world. Elevated CO_2 levels were found to reduce the overall concentration of 25 important minerals—including calcium, potassium, zinc, and iron—in plants by 8% on average. Furthermore, Loladze found that an increased exposure to CO_2 also increased the ratio of carbohydrates to minerals in these plants.

This reduction in the nutritional value of plants could have profound impacts on human health: a diet that is deficient in minerals and other nutrients can cause malnutrition, even if a person consumes enough calories. This type of malnutrition is common around the world because many people eat only a limited number of staple crops, and do not eat enough foods that are rich in minerals, such as fruits, vegetables, dairy and meats. Diets that are poor in minerals (in particular, zinc and iron) lead to reduced growth in childhood, to a reduced ability to fight off infections, and to higher rates of maternal and child deaths.

Loladze argues that these changes might contribute to the rise in obesity, as people eat increasingly starchy plant-based foods, and eat more to compensate for the lower mineral levels found in crops. Looking to the future, these findings highlight the importance of breeding food crops to be more nutritious as the world's CO_2 levels continue to rise.

DOI: 10.7554/eLife.02245.002

multiple nutritional currencies, for example macronutrients (carbohydrates, protein, and fat) and micronutrients (minerals, vitamins and phytonutrients). Assessing relative changes within and among multiple currencies requires significantly more effort and funding than measuring only plant quantity (e.g., yield). Second, plant quality, including the plant ionome—all the minerals and trace-elements found in a plant (*Lahner et al., 2003*; *Salt et al., 2008*)—is inherently variable; and measurement imprecisions further amplify the variability. For example, *Stefan et al. (1997)* report the accuracy test for 39 facilities that analyzed samples of the same plant tissues: the inter-laboratory variance was 6.5% for N, but twice as large for phosphorus (P) and calcium (Ca), and reached 130% for sodium (Na). Therefore, CO_2-induced changes in the plant ionome (the signal) can be easily lost amid highly variable data (the noise), especially when such data are limited and sample sizes are small. However, it is important to bear in mind that a low signal-to-noise ratio *does not* imply that the signal is practically insignificant, especially if it is global and sustained—a point revisited in the 'Discussion'.

Elusive CO_2 effect on the plant ionome: contradictory findings

The first empirical evidence of lower mineral content in plants exposed to eCO_2 appeared at least over a quarter century ago (e.g., *Porter and Grodzinski, 1984*; *Peet et al., 1986*; *O'Neill et al., 1987*). Physiological mechanisms responsible for the overall decline of plant mineral content—with expected changes being *non-uniform* across minerals—have been proposed: the increased carbohydrate production combined with other eCO_2 effects such as reduced transpiration (*Loladze, 2002*; *McGrath and Lobell, 2013*). However, most of the experimental evidence showing CO_2-induced mineral declines came from artificial facilities, mainly closed chambers and glasshouses, and many results were statistically non-significant. This led some research groups to challenge altogether the notion of lower mineral content in plants exposed to eCO_2 in field conditions. Such conditions are most accurately represented in Free-Air Carbon dioxide Enrichment (FACE) centers, which have been established in at least 11 countries.

In the grains of rice harvested at four FACE paddies in Japan, *Lieffering et al. (2004)* found no decline in any of the minerals but lower N content. The result disagreed with *Seneweera and Conroy (1997)*, who were the first to report lower iron (Fe) and zinc (Zn) in grains of rice grown at eCO_2 and warned that altered rice quality can negatively affect developing countries. *Lieffering et al. (2004)*, however, argued that the result of *Seneweera and Conroy (1997)* could be an artifact of growing rice in pots, which restrict rooting volumes. They hypothesized that in FACE studies, which provide unrestricted rooting volumes, plants would increase uptake of all minerals to balance the increased carbohydrate production. This hypothesis, however, found no support in the FACE studies of *Pang et al. (2005)* and *Yang et al. (2007)* (carried out in China and latitudinally not very far from the study in Japan), who found that eCO_2 significantly altered the content of several minerals in rice grains.

The contradictory results coming from these studies on rice seem perplexing, especially in light of the very robust effect that eCO_2 has on N in non-leguminous plants. Elevated CO_2 reduces N concentrations by 10–18% systemically throughout various tissues: leaves, stems, roots, tubers, reproductive and edible parts, including seeds and grains (*Cotrufo et al., 1998*; *Jablonski et al., 2002*; *Taub et al., 2008*). If the increased carbohydrate production dilutes the nutrient content in plants, why does the dichotomy seem to exist between the responses of N and minerals to eCO_2? In addition to the carbohydrate dilution and reduced transpiration, eCO_2 can further lower N concentrations in plants by: (1) reducing concentrations of Rubisco—one of the most abundant proteins on Earth that comprises a sizable N-pool in plants (*Drake et al., 1997*), and (2) inhibiting nitrate assimilation (*Bloom et al., 2010*). Hence, it is reasonable to expect the effect of eCO_2 on N to be larger and, thus, easier to discern than its effect on most minerals. The stronger signal for N, combined with the plentiful and less noisy data on this element, can help explain why by the end of last century the effect of eCO_2 on N had been already elucidated (*Cotrufo et al., 1998*), but its effect on minerals has remained elusive.

The obscure nature of the effect of eCO_2 on minerals becomes particularly apparent in the largest to date meta-analysis on the issue by *Duval et al. (2011)*, who fragmented data from 56 eCO_2 studies into 67 cases. In 47 of the cases, the effect of eCO_2 on minerals was statistically non-significant, that is the 95% Confidence Interval (CI) for the effect size overlapped with 0. The remaining 20 cases were statistically significant but showed no pattern: for example, Fe increased in grasses but decreased in trees, Zn increased in roots but decreased in stems, while in grains only sulfur (S) decreased. *Duval et al. (2011)* concluded: "A major finding of this synthesis is the lack of effect of CO_2 on crop grains nutrient concentration". This would imply laying to rest the hypothesis that eCO_2 consistently alters the plant ionome and would render mitigation efforts to combat declining crop mineral concentrations in the rising CO_2 world unnecessary. However, a closer examination of the results of *Duval et al. (2011)* reveals that every statistically significant increase in mineral concentrations was obtained by bootstrapping a sample of size 2, 4 or 5—a recipe for generating invalid 95% CIs. *Ioannidis (2005)* showed that false research findings, stemming from small sample sizes and associated low statistical power, are a persistent problem in biomedical sciences.

'Power failure' and the plant ionome

Calling the problem as 'power failure', *Button et al. (2013)* emphasized that the probability of a research finding to reflect a true effect drops drastically if the statistical power is reduced from 0.80 (considered as appropriate) to low levels, for example <0.30. Since the power of a statistical test drops non-linearly with the effect size, a sample size that is sufficient for detecting a 15% effect, for example a decline in N content, can be inadequate for detecting a 5% effect, for example a decline in a mineral content. Considering that the standard deviation of mineral concentrations in a plant tissue can reach 25% (*Duquesnay et al., 2000*; *Lahner et al., 2003*), the 5% effect size standardized as Cohen's d is $d = 5/25 = 0.2$. A t test applied for $d = 0.2$ to a sample size of 3–5—a typical size used in eCO_2 studies—yields the power of 0.06–0.10 (*Faul et al., 2007*). (Unfortunately, *MetaWin* (*Rosenberg et al., 2000*), a statistical package routinely used in meta-analytic and other CO_2 studies in ecology, provides neither a priori nor *post-hoc* power estimates.) Such a small power not only raises the probability of obtaining a false negative to 90–94% but also increases the likelihood that a statistically significant result does not reflect a true effect (*Button et al., 2013*).

Answering questions with adequate power

As of this writing, researchers on four continents have generated data sufficient for answering with an adequate statistical power, the following questions:

1. Does eCO_2 shift the plant ionome? If yes, what are the direction and magnitude of shifts for individual chemical elements? How does the effect of eCO_2 on N compares to its effect on minerals?
2. Do FACE studies differ principally from non-FACE studies in their effect on the plant ionome?
3. Do the plant ionomes in temperate and subtropical/tropical regions differ in their response to eCO_2?
4. Do the ionomes of photosynthetic tissues and edible parts differ in their response to eCO_2? How does eCO_2 affect the ionomes of various plant groups (woody/herbaceous, wild/crops, C_3/C_4) and grains of the world's top C_3 cereals—wheat, rice, and barley?

Results

For brevity, hereafter 'minerals' refer to all elements except C, hydrogen (H), oxygen (O), and N. All results are for C_3 plants except when noted otherwise.

Power analysis

Plotting the effect sizes (with 95% CIs) for the 25 minerals against their respective statistical power reveals a clear pattern (*Figure 1*). In the very low power (<0.20) region, the noise completely hides the CO_2-induced shift of the plant ionome. In the low power region (<0.40), the shift still remains obscure. As the statistical power increases, so does the likelihood that a statistically significant result reflects true effect and, consequently, the direction and the magnitude of the CO_2 effect on minerals become increasingly visible in the higher power regions of the plot.

To increase the likelihood of reporting true effects, only results with the statistical power >0.40 are reported in this section. However, *Figure 1–source data 1* lists all the results together with their p-values irrespective of the statistical power (e.g., results for chromium (Cr) or the bean ionome are not shown here due to low power, but are listed in *Figure 1–source data 1*).
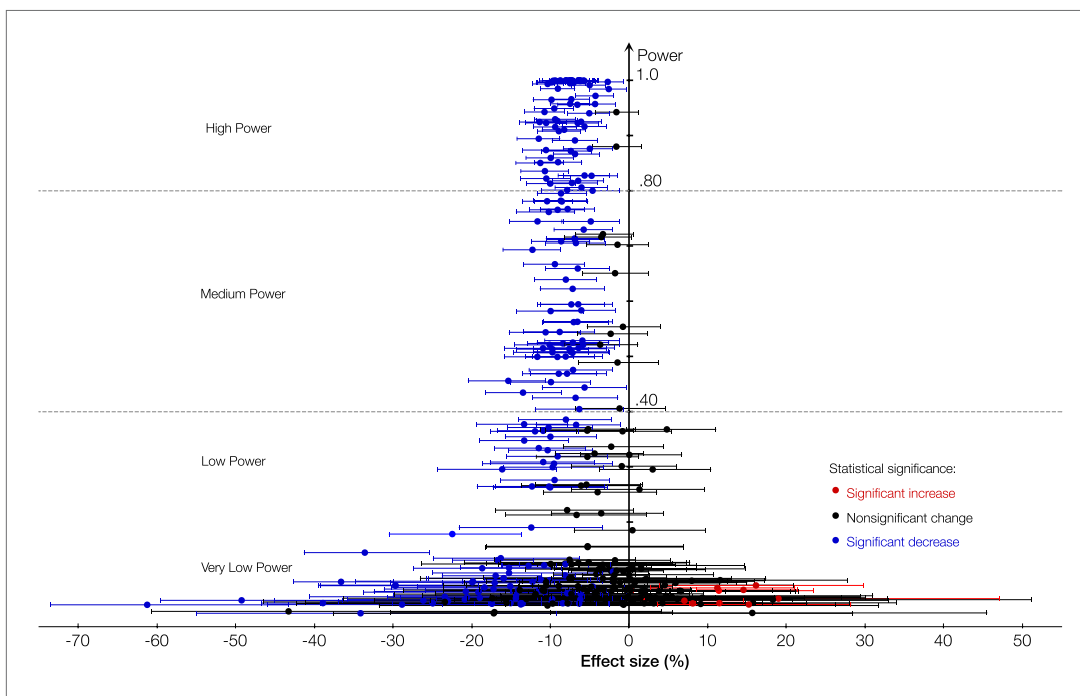
Figure 1. Statistical power and the effect of CO_2 on the plant ionome. The effect of elevated atmospheric CO_2 concentrations (eCO_2) on the mean concentration of minerals in plants plotted (with the respective 95% confidence intervals [CI]) against the power of statistical analysis. The figure reflects data on 25 minerals in edible and foliar tissues of 125 C_3 plant species and cultivars. The true CO_2 effect is hidden in the very low and the low power regions. As the statistical power increases, the true effect becomes progressively clearer: the systemic shift of the plant ionome.
DOI: 10.7554/eLife.02245.003

The following source data are available for figure 1:

Source data 1. Supportive data for *Figures 1–8*.
DOI: 10.7554/eLife.02245.015

CO₂ effect on individual elements

Across all the data, eCO₂ reduced concentrations of P, potassium (K), Ca, S, magnesium (Mg), Fe, Zn, and copper (Cu) by 6.5–10% ($p<0.0001$) as shown on *Figure 2*. Across all the 25 minerals, the mean change was (−8%, −9.1 to −6.9, $p<0.00001$). Only manganese (Mn) showed no significant change. It is not clear whether the oxygen-evolving complex (OEC) demands for Mn separate this mineral from the pattern of declines exhibited by other minerals. Among all the measured elements, only C increased (6%, 2.6 to 10.4, $p<0.01$). The sharp difference between the responses of C and minerals to eCO₂ is expected if a higher carbohydrate content drives the change in the plant ionome: for most plant tissues, the dilution by carbohydrates lowers the content of minerals while having little effect on C (*Loladze, 2002*). (This also suggests that the increase in C concentrations found here could be a result of a higher content of lipids or lignin—the two sizable plant compounds that are very C-rich [~60–75% C].)

The patterns of change within edible and foliar tissues are similar: N, P, Ca, Mg, Zn, and Cu declined significantly in both tissues (*Figures 3, 4*). Aside from Mn, only K showed no significant decline in the
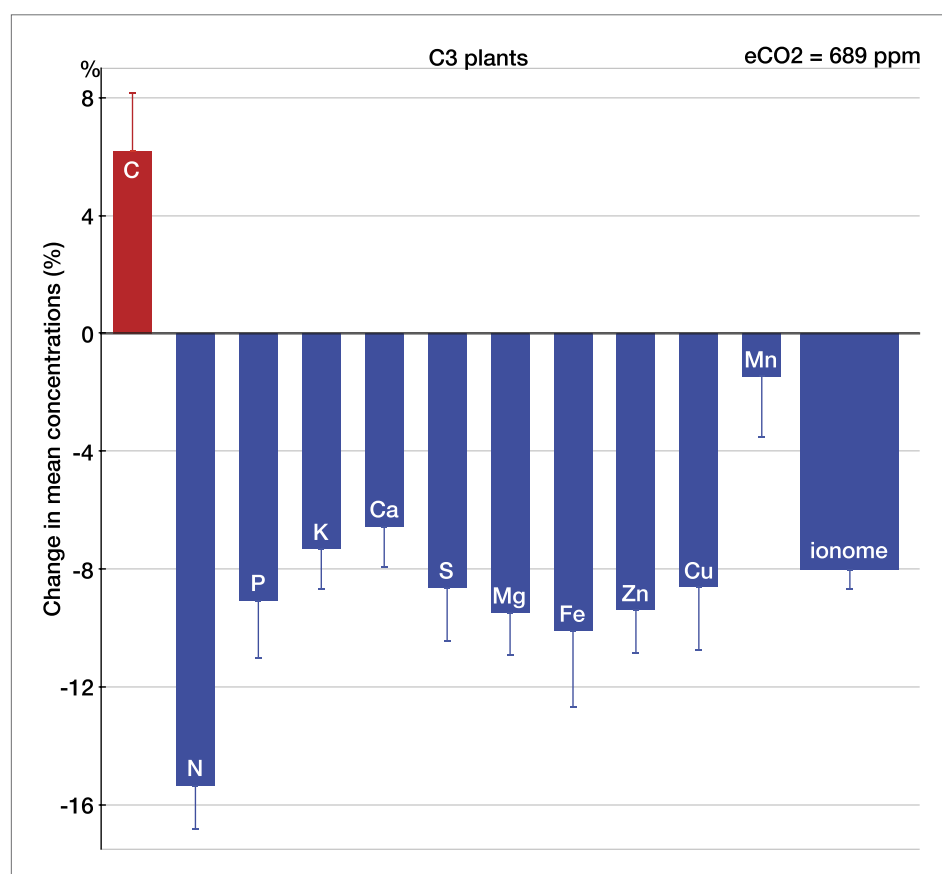
Figure 2. The effect of CO₂ on individual chemical elements in plants. Change (%) in the mean concentration of chemical elements in plants grown in eCO₂ relative to those grown at ambient levels. Unless noted otherwise, all results in this and subsequent figures are for C₃ plants. Average ambient and elevated CO₂ levels across all the studies are 368 ppm and 689 ppm respectively. The results reflect the plant data (foliar and edible tissues, FACE and non-FACE studies) from four continents. Error bars represent the standard error of the mean (calculated using the number of *mean* observations for each element). The number of mean and total (with all the replicates) observations for each element is as follows: C(35/169), N(140/696), P(152/836), K(128/605), Ca(139/739), S(67/373), Mg(123/650), Fe(125/639), Zn(123/702), Cu(124/612), and Mn(101/493). An element is shown individually if the statistical power for a 5% effect size for the element is >0.40. The 'ionome' bar reflects all the data on 25 minerals (all the elements in the dataset except for C and N). All the data are available at Dryad depository and at GitHub. Copies of all the original sources for the data are available upon request.
DOI: 10.7554/eLife.02245.004
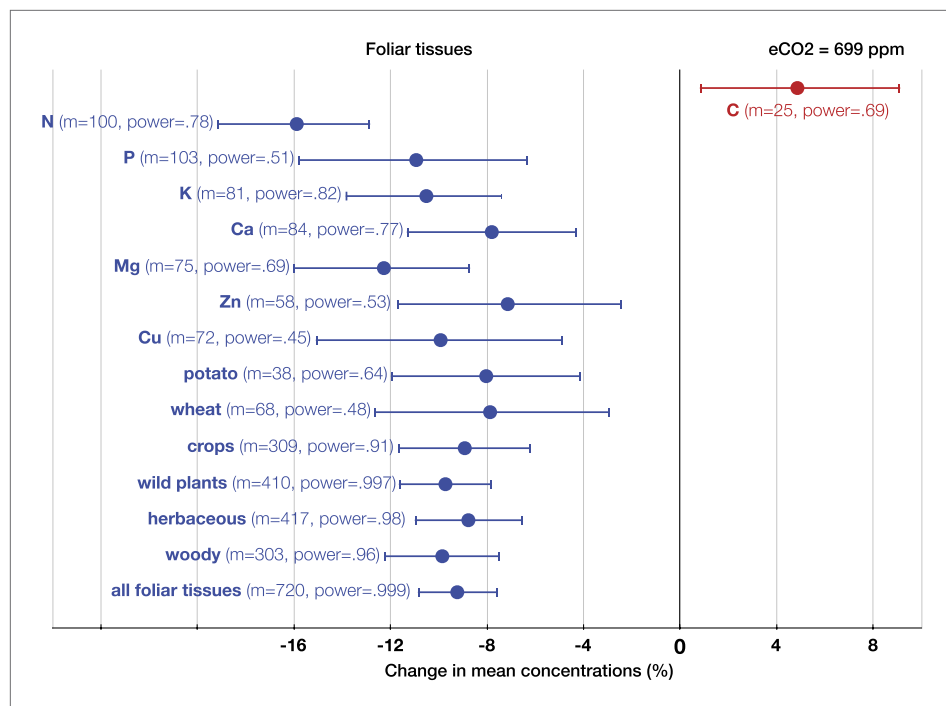
Figure 3. The effect of CO_2 on foliar tissues. Change (%) in the mean concentration of chemical elements in foliar tissues grown in eCO_2 relative to those grown at ambient levels. Average ambient and eCO_2 levels across all the foliar studies are 364 ppm and 699 ppm respectively. Error bars represent 95% CI. For each element, the number of independent mean observations, m, is shown with the respective statistical power. For each plant group, m equals the sum of mean observations over all the minerals (not including C and N) for that group. Elements and plant groups for which the statistical power is >0.40 (for a 5% effect size) are shown.
DOI: 10.7554/eLife.02245.005

edible tissues (on *Figure 1*, it is visible as one of the only two black 95% CI in the 'High Power' region). In the foliar tissues, Mg declined the most (−12.3%, −16 to −8.7), which is congruent with the hypothesis of *McGrath and Lobell (2013)* that Mg should exhibit a larger decline in photosynthetic tissues because 'chlorophyll requires a large fraction of total plant Mg, and chlorophyll concentration is reduced by growth in elevated CO_2'. However, the 95% CIs for Mg and for most other minerals overlap. A richer dataset would shed more light on the issue of Mg in photosynthetic tissues.

As expected, among all elements N declined the most (−15%, −17.8 to −13.1, p<0.00001) (*Figure 2*), matching very closely previous findings (*Figures 3–6*): the 17–19% decline in leaves found by *Cotrufo et al. (1998)* and the 14% decline in seeds found by *Jablonski et al. (2002)*. Since the contents of N and protein correlate strongly in plant tissues, the lower N in edible tissues (*Figure 4*) corroborates the protein declines in crops found by *Taub et al. (2008)*.

FACE vs non-FACE studies

With respect to the types of experiments, the CO_2 effect on the plant ionome is surprisingly robust: in both the FACE and the non-FACE studies eCO_2 significantly reduced N, P, K, Ca, S, Mg, and Zn (*Figures 5, 6*). The high cost of CO_2 required for running free-air experiments led to a much lower average level of eCO_2 in the FACE studies (560 ppm) cf. 732 ppm in the non-FACE studies. It is plausible that the lower levels of CO_2 in the FACE studies contributed to a smaller overall mineral decline (−6.1%, −7.8 to −4.4) cf. (−8.7%, −10.1 to −7.4) for the non-FACE studies. In both the FACE and the non-FACE studies, the overall mineral concentrations declined significantly in herbaceous plants and crops, foliar and edible tissues, including wheat and rice (*Figures 5, 6*).

Geographical analysis

The CO_2 effect on the plant ionome appears to be pervasive throughout latitudes (*Figures 7, 8*). With the exception of three small centers (in Bangladesh, Japan, and the UK), the mean mineral concentrations
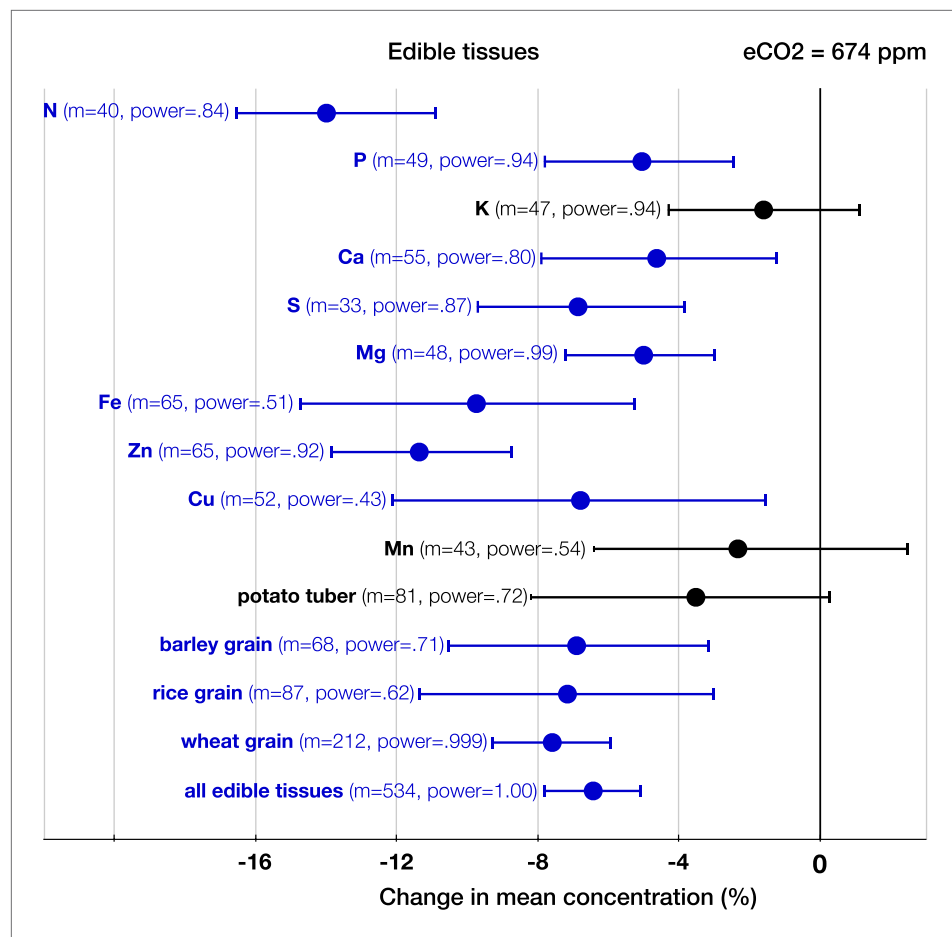
Figure 4. The effect of CO_2 on edible tissues. Change (%) in the mean concentration of chemical elements in edible parts of crops grown in eCO_2 relative to those grown at ambient levels. Average ambient and elevated CO_2 levels across all the crop edible studies are 373 ppm and 674 ppm respectively. Other details are in the legends for **Figures 2 and 3**. DOI: 10.7554/eLife.02245.006

declined in every FACE and open top chamber (OTC) center on four continents. The mineral decline in the tropics and subtropics (−7.2%, −10.4 to −4.0, p<0.0001) is comparable to the decline in the temperate region (−6.4%, −7.9 to −5.0, p<0.00001). A finer regional fragmentation currently is not possible due to lack of data for Africa, South America, Russia, and Canada. For many existing centers the data are limited and yield a low statistical power.

Germany leads the world in the FACE and OTC data generation with the largest number of *mean* observations of mineral concentrations (285), followed by the USA (218) (**Figure 8**). Though Australia generated only 30 mean observations, it stands out in the exceptional precision of some of its studies: the wheat experiments of **Fernando et al. (2014)** employed an unprecedented for FACE studies 48 replicates (for this reason, the study is easily identifiable on **Figure 9**).

CO_2 effect on various plant groups and tissues

Since eCO_2 does not stimulate carbohydrate production in C_4 plants to a degree that it does in C_3 plants, one would expect a milder CO_2 effect on minerals for C_4 plants. Indeed, no statistically significant effect was found on the ionome of C4 plants (**Figure 8**). Note, however, that the very limited data on this plant group are insufficient for deducing the absence of the effect; rather, it is likely that the effect size <5% for C_4 plants.

The CO_2 effect on the C_3 plant ionome shows its systemic character through the analysis of various plant groups and tissues (**Figures 3, 4 and 8**). Elevated CO_2 reduced the overall mineral concentrations in crops (−7.2%, −8.6 to −5.6); wild (−9.7%, −11.6 to −7.8), herbaceous (−7.5%, −8.7 to −5.6), and woody (−9.6%, −12.1 to −7.6) plants; foliar (−9.2%, −10.8 to −7.6) and edible (−6.4%, −7.8 to −5.1)
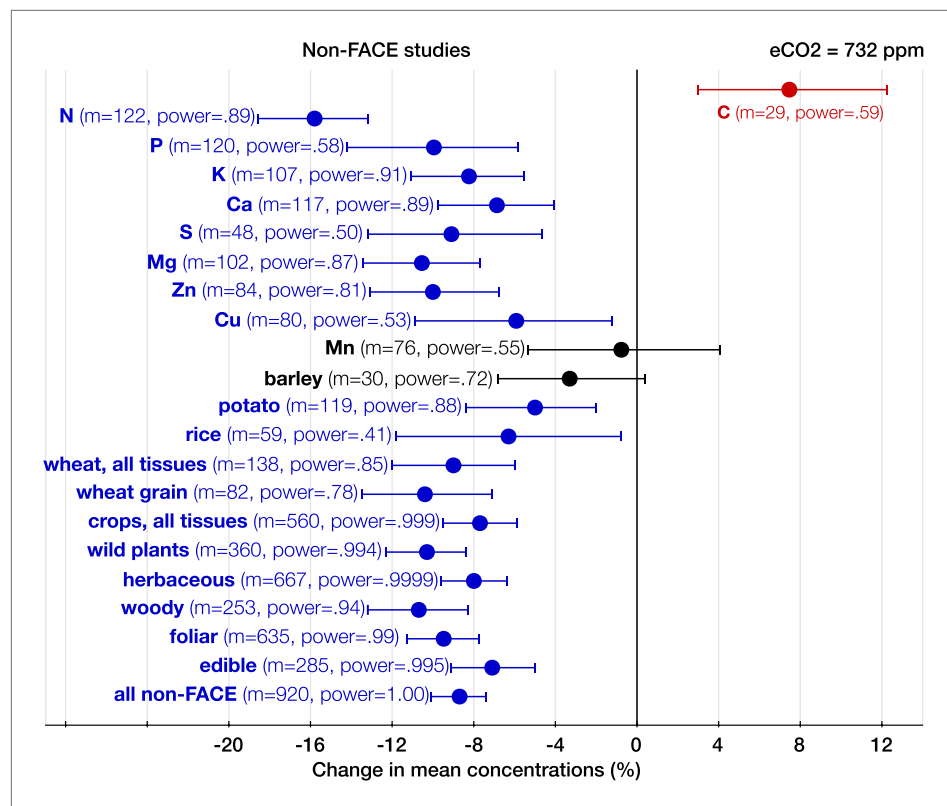
Figure 5. The effect of CO_2 in artificial enclosures. Change (%) in the mean concentration of chemical elements of plants grown in chambers, greenhouses, and other artificial enclosures under eCO_2 relative to those grown at ambient levels. Average ambient and eCO_2 levels across all the non-FACE studies are 365 ppm and 732 ppm respectively. Other details are in the legends for *Figures 2 and 3*.
DOI: 10.7554/eLife.02245.007

tissues, including grains (−7.2%, −8.6 to −5.6). The cereal specific declines in *grains* are as follows: wheat (−7.6%, −9.3 to −5.9), rice (−7.2%, −11.3 to −3.1), and barley (−6.9%, −10.5 to −3.2) (*Figure 8*). This is notable because wheat and rice alone provide over 40% of calories to humans.

Discussion

The analysis of all the data shows that eCO_2 shifts the plant ionome toward lower mineral content; the mean change across all the 25 measured minerals is (−8%, −9.1 to −6.9) (*Figure 2*). This shift, however, is hidden from low-powered statistical tests (*Figure 1*). Attaining adequate meta-analytic power reveals that the shift is:

1. Empirically robust—evident in both artificial (chambers, greenhouses) and field (FACE) conditions (*Figures 5 and 6*).
2. Geographically pervasive—found in temperate and subtropical/tropical regions (*Figures 7 and 8*).
3. Systemic—affecting herbaceous and woody plants, crops, and wild plants, photosynthetic and edible tissues, including wheat, rice, and barley grains (*Figures 3, 4 and 8*).

Elevated CO_2 alters plant C:N:P:S stoichiometry

Not only does eCO_2 reduce the plant mineral content, but it also alters plant stoichiometry. Specifically, the effect of eCO_2 on N is nearly twice as large as its mean effect on minerals. The differential effect of eCO_2 on N (15%), and P (9%) and S (9%) translates into a ~7% reduction in the plant N:P and N:S. In contrast to the lower N and mineral content, eCO_2 increased C content by 6% (*Figures 2, 3 and 5*). It follows then that eCO_2 increases C:P and C:S by 16%, and C:N by 25% confirming the previous findings of 19–27% higher C:N in plants grown in eCO_2 (*Poorter et al., 1997*; *Stiling and Cornelissen, 2007*; *Robinson et al., 2012*).
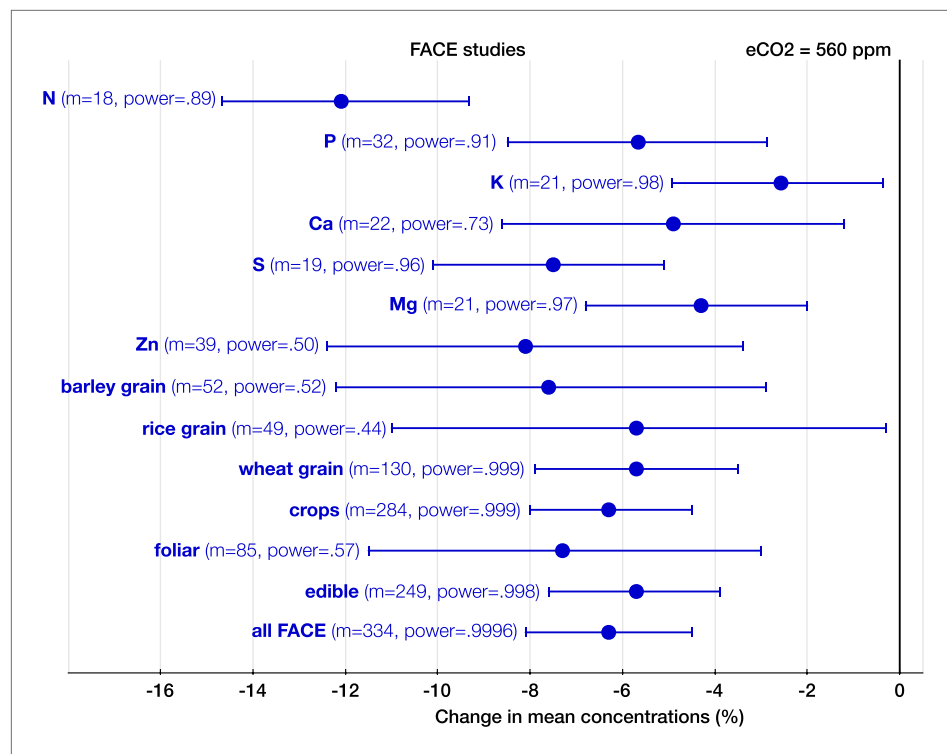
Figure 6. The effect of CO_2 at FACE centers. Change (%) in the mean concentration of chemical elements of plants grown in Free-Air Carbon dioxide Enrichments (FACE) centers relative to those grown at ambient levels. Average ambient and eCO_2 levels across all the FACE studies are 376 ppm and 560 ppm respectively. Other details are in the legends for *Figures 2 and 3*.
DOI: 10.7554/eLife.02245.008

Data scarcity

The current dataset (available at Dryad depository) suffices to show the overall shift in the plant ionome. However, it would require much richer datasets to quantify differences among the shifts of various minerals and to assess shifts in the ionomes of individual species. Unfortunately, funding hurdles for analyzing fresh and archived samples harvested at FACE centers have significantly delayed progress in this area. Only two CO_2 studies report selenium (Se) content (*Högy et al., 2009*, *2013*), and none report data on tin (Sn), lithium (Li), and most other trace-elements. For many of the world's popular crops, pertinent data are non-existent or very limited, including (in the descending order of calories provided to the world's population, *FAO, 2013*): maize (the top C_4 crop), soybeans (including oil), cassava, millet, beans, sweet potatoes, bananas, nuts, apples, yams, plantains, peas, grapes, rye, and oats.

The current data scarcity, however, should not detract our attention from what is likely to be the overarching physiological driver behind the shift in the plant ionome—the CO_2-induced increase in carbohydrate production and the resulting dilution by carbohydrates. Let us take a closer look at this nutritionally important issue.

TNC:protein and TNC:minerals respond strongly to elevated CO_2

Carbohydrates in plants can be divided into two types: total structural carbohydrates (TSC; e.g., cellulose or fiber) that human body cannot digest, and total non-structural carbohydrates (TNC), most of which—including starch and several sugars (fructose, glucose, sucrose, and maltose)—is readily digestible and absorbed in the human gut. Hence, for humans, TNC carries the most of caloric and metabolic load of carbohydrates. Out of the two types of carbohydrates, eCO_2 affects stronger the latter, boosting TNC concentration by 10–45% (*Stiling and Cornelissen, 2007*; *Robinson et al., 2012*). Furthermore, eCO_2 tends to lower protein in plant tissues (*Taub et al., 2008*). Hence, we can reason that eCO_2 should exacerbate the inverse relationship found between TNC and protein
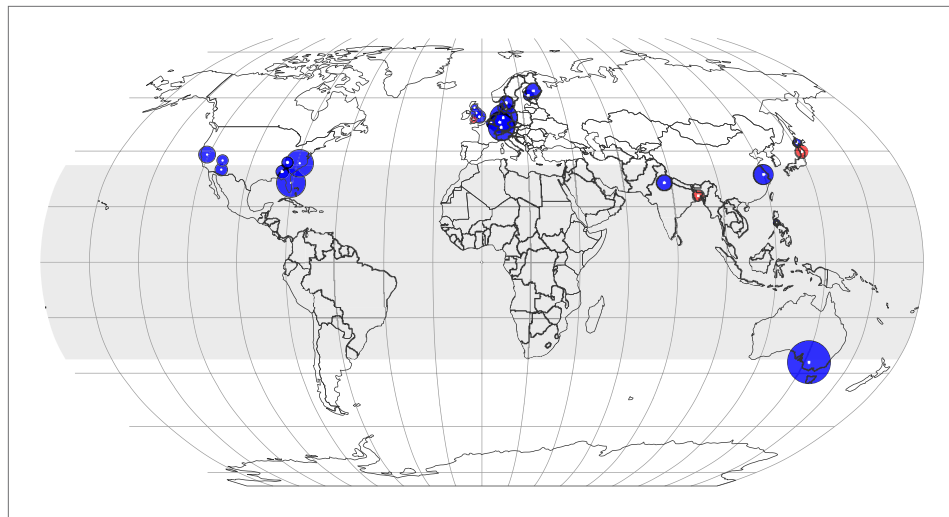
Figure 7. The effect of CO_2 at various locations and latitudes. Locations of the FACE and Open Top Chamber (OTC) centers, which report concentrations of minerals in foliar or edible tissues, are shown as white dots inside colored circles. The area of a circle is proportional to the total number of observations (counting replicates) generated by the center. If the mean change is negative (decline in mineral content), the respective circle is blue; otherwise, it is red. The figure reflects data on 21 minerals in 57 plant species and cultivars. The shaded region (between 35 N and S latitudes) represents tropics and subtropics.
DOI: 10.7554/eLife.02245.009

(*Poorter and Villar, 1997*). Considering that TNC and protein are two out of the three primary macro-nutrients (with fats/lipids being the third), it becomes imperative to quantify changes in TNC:protein, when estimating the impact of altered plant quality on human nutrition in the rising CO_2 world.

Regrettably, TNC:protein is rarely reported by CO_2 studies; instead C:N is used as a yardstick for accessing changes in the plant quality. However, C:N poorly correlates with TNC:protein because protein is more C-rich than carbohydrates (C content in protein is 52–55% cf. 40–45% in carbohydrates). Thus, a *higher* carbohydrate:protein results in a *lower* C content. This means that CO_2-induced changes in nutritionally and metabolically important ratios—TNC:protein and TNC:minerals—can substantially exceed the respective changes in C:N. We can calculate changes in TNC:protein using reported changes in TNC and protein (see 'Formula for calculating percentage changes in TNC:protein and TNC:minerals' in 'Materials and methods'). *Table 1* compares CO_2-induced changes in C:N with respective changes in TNC:protein. It shows that eCO_2 can elevate TNC:protein up to fivefold higher than it does C:N.

How shifts in TNC:protein affect human nutrition is still unknown. New evidence, however, challenges "the notion that a calorie is a calorie from a metabolic perspective" by showing that changes in dietary carbohydrate:protein:fat ratios affect metabolism and weight gain in humans (*Ebbeling et al., 2012*). The new evidence supports an emerging view that while obesity is quantified as an imbalance between energy inputs and expenditures (*Hall et al., 2011*), it could also be a form of malnutrition (*Wells, 2013*), where increased carbohydrate:protein (*Simpson and Raubenheimer, 2005*) and excessive carbohydrate consumption (*Taubes, 2013*) could be possible culprits.

Absolute CO_2 effect on TNC. Spoonful of sugars for everyone?

The baseline TNC content in plant tissues varies widely. In grains and tubers, it is very high, 50–85% of dry mass (DM). Therefore, in these tissues a percentage increase in TNC is arithmetically limited (e.g., a 60% increase is impossible). However, even a modest percentage increase in TNC-rich tissues can be nutritionally meaningful in absolute terms. For example, the FACE study of *Porteaus et al. (2009)* reports a 7–8% increase in starch concentrations in wheat grains, which translates to ~4 g of additional starch per 100 g DM. In contrast to grains and tubers, the baseline TNC level in photosynthetic tissues is small (usually <25%), which makes large TNC increases possible. For example, *Teng et al. (2006)* reports that eCO_2 increased TNC by 76% in leaves of *Arabidopsis thaliana*. What is interesting here is that in *absolute* terms (per 100 g DM) the ~5 g TNC increase in *Arabidopsis thaliana* is comparable to the ~4 g TNC increase in wheat grains.
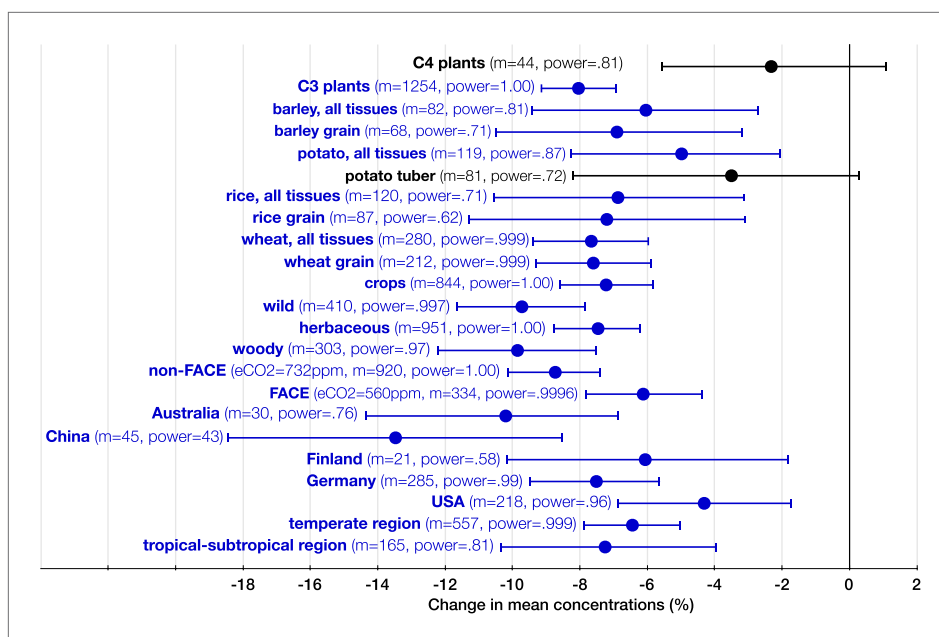
Figure 8. The systemic aspect of the CO_2 effect. Change (%) in the mean concentration of minerals in plants grown in eCO_2 relative to those grown at ambient levels. All the results in the figure reflect the combined data for the foliar and the edible tissues. The number of total *mean* observations (*m*) for all the measured minerals across all the studies for each crop/plant group, experiment type, country, or region is shown with the respective statistical power. Country specific and regional results reflect all the FACE and Open Top Chamber (OTC) studies carried in any given country/region. The number of total observations (with replicates) for all the minerals (not counting C and N) for each country is as follows: Australia (926), China (193), Finland (144), Germany (908), and USA (1156). Other details are in the legends for *Figures 2 and 3*.
DOI: 10.7554/eLife.02245.010

More generally, CO_2 studies show that—irrespective of the baseline TNC content—eCO_2 tends to boost TNC by a few grams (1–8 g) per 100 g DM of plant tissue (*Poorter et al., 1997*; *Keutgen and Chen, 2001*; *Katny et al., 2005*; *Erbs et al., 2010*; *Azam et al., 2013*). Note that such an infusion of carbohydrates into plant tissues, all else being equal, dilutes the content of other nutrients by ~1–7.4%. Let us compare the dilution with its pragmatic and easily graspable analog—adding a spoonful of sugar-and-starch mixture. *Table 2* shows that the CO_2 effect on TNC:protein and TNC:minerals is stoichiometrically similar to the effect of adding a spoonful of carbohydrates to every 100 g DM of plant tissue.

Clearly, adding a spoonful of sugar sporadically to one's diet is not a cause for concern. However, the inescapable pervasiveness of globally rising atmospheric CO_2 concentrations raises new questions: What are health consequences, if any, of diluting every 100 g DM of raw plant products with a spoonful of starch-and-sugar mixture? What are the consequences if the dilution is not sporadic but unavoidable and lifelong? These questions are better left for nutritionists, but it is worth noting that *WHO (2014)* conditionally recommends that intake of free sugars not exceed 5% of total energy, which is equivalent to 5–8 teaspoons of sugar for a typical 2000–3000 kcal/day diet.

Below, I shift focus on a direct consequence of the CO_2-induced increase in carbohydrate production—the mineral decline in plant tissues, and explore its potential effect on human nutrition.

Plant minerals and 'hidden hunger'

'Hidden hunger'—stems from poorly diversified plant-based diets meeting caloric but not nutritional needs. It is currently the world's most widespread nutritional disorder (*Kennedy et al., 2003*; *Welch and Graham, 2005*). It lowers the GDP of the most afflicted countries by 2–5% and is partly responsible for their Third World status (*WHO, 2002*; *Stein, 2009*). A paradoxical aspect of 'hidden hunger' is that the minuscule amount of minerals, which a human body requires, could be provided easily and inexpensively—at least in theory—to all people in need by fortifying foods with minerals. However, in practice, such required mineral levels do not reach large parts of the world's community.
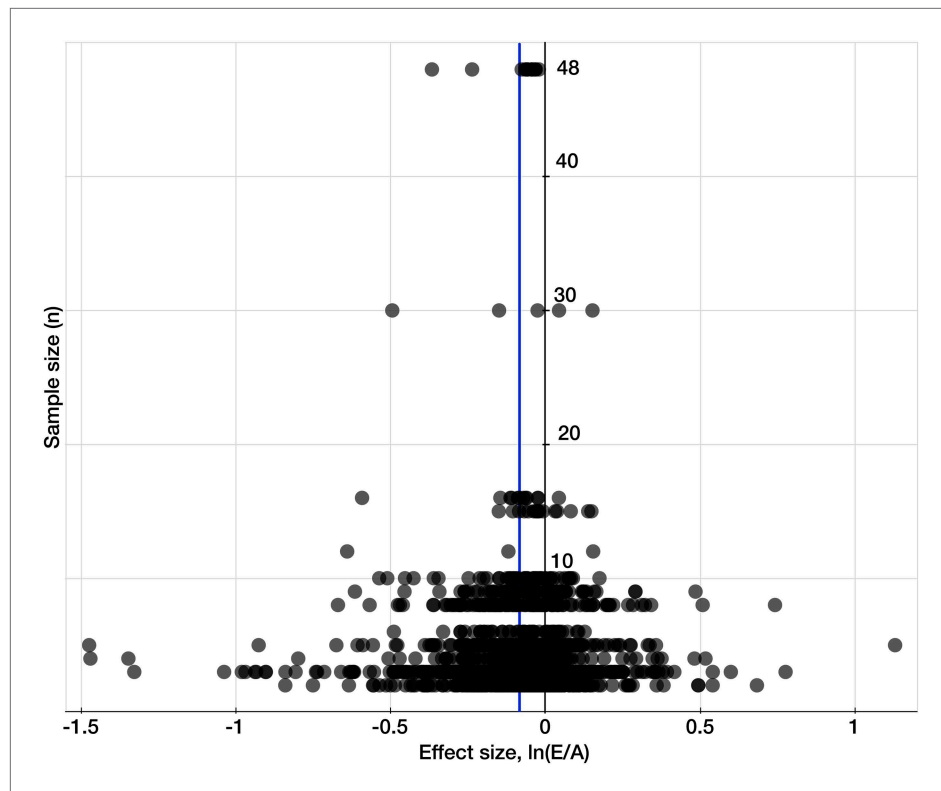
Figure 9. Testing for publication bias. A funnel plot of the effect size (the natural log of the response ratio) plotted against the number of replicates/sample sizes (*n*) for each study and each mineral in the dataset for C_3 plants. The plot provides a simple visual evaluation of the distribution of effect sizes. The blue line represents the mean effect size of eCO$_2$ on mineral concentrations: the decline of 8.39% (yielding the decline of 8.04% when back transferred from the log-form). The symmetrical funnel shape of the plot around the mean effect size indicates the publication bias in the dataset is insignificant (***Egger et al., 1997***).
DOI: 10.7554/eLife.02245.011

The case of iodine is illustrative: although iodized table salt nearly wiped out iodine deficiency in the industrialized world, a billion people still have no regular access to it, making iodine deficiency the leading cause of preventable brain damage, cretinism, and lower IQ in children (***Welch and Graham, 1999***; ***WHO, 2002***). Hence, the reality of logistic, economic, and cultural hurdles for fortification leaves the natural and bioavailable mineral content in food, and in plants in particular, to be the major, and sometimes the only, consistent mineral supply for a large part of mankind (***White and Broadley, 2009***; ***Bouis and Welch, 2010***). This supply, unfortunately, is suboptimal for human nutrition with some of the consequences outlined below.

Every third person in the world is at risk of inadequate Zn intake with its deficiency substantially contributing to stunting, compromised immunity, and child mortality (***Brown et al., 2001***; ***UNICEF, 2009***). Iron deficiency affects at least 2 billion people and is the leading cause of anemia that increases maternal mortality (***WHO, 2002***; ***UNICEF, 2009***). Millions are Ca, Mg, and Se deficient (***Stein, 2009***; ***White and Broadley, 2009***), including some population segments of developed countries (***Rayman, 2007***; ***Khokhar et al., 2012***). Ironically, a person can be obese *and* mineral undernourished—the so called 'hunger-obesity paradox' (***Scheier, 2005***), for example the many homeless in the US who rely on "cheap and energy-dense but low-nutrient" foods (***Koh et al., 2012***). With every third adult in the world being overweight or obese (***Keats and Wiggins, 2014***), WHO ranks both mineral undernutrition and obesity among the top 20 global health risks (***WHO, 2002***; ***Hill et al., 2003***; ***Stein, 2009***). While the role of mineral deficiency in obesity is still unclear, intriguing links have been found between the lower blood serum concentrations of Ca, Cr, Fe, Mg, Mn, Se, Zn, and increased body mass index (BMI), with most of the findings appearing in the last decade (***Singh et al., 1998***; ***Martin et al., 2006***; ***Arnaud et al., 2007***; ***García et al., 2009***; ***Payahoo et al., 2013***; ***Yerlikaya et al., 2013***).

Table 1. Comparing the effects of CO_2 on two plant quality indicators.

Study/species	C:N (%)	TNC:protein (%)	Reference
Arabidopsis thaliana	25	125	*Teng et al. (2006)*
Bromus erectus	6	26	*Roumet et al. (1999)**
Dactylis glomerata	17	53	*Roumet et al. (1999)**
wheat grain (low N)	−10	47	*Porteaus et al. (2009)*
wheat grain (high N)	−18	7	*Porteaus et al. (2009)*
wheat grain	9	6	*Högy et al. (2009)*
27 C_3 species	28	90	*Poorter et al. (1997)*
meta-analysis	25	54	*Robinson et al. (2012)*
meta-analysis	27	39	*Stiling and Cornelissen (2007)*

CO_2-induced changes (%) in C:N (a quality indicator often used in CO_2 studies) and in TNC:protein (a rarely used but nutritionally important indicator) for wheat grains and for foliar tissues of various plants. The results shows that in the same plant tissue, eCO_2 can increase TNC:protein up to several-fold > C:N. Significant CO_2-induced shifts in the ratio of major macronutrients are probable. Hence, it is important for CO_2 studies to start accessing and reporting changes in TNC:protein.
*in lieu of protein, N content is used.
DOI: 10.7554/eLife.02245.012

How can the CO_2-induced depletion of minerals in crops affect humans? I emphasize that the impact of CO_2-induced shifts in the quality of crops on human health is far from settled. The purpose of what follows is not to make definitive claims but to stimulate research into this important but unresolved issue.

Table 2. Comparing the effect of CO_2 to the effect of adding 'a spoonful of sugars.'

Plant quality indicator	Effect of adding 5g of TNC (%)	Effect of elevated CO_2 (%)
Grains and tubers:		
TNC	2.6	1 to 15
TNC:protein	7	6 to 47
TNC:minerals	7	6 to 28
protein	−4.8	−14 to −9
minerals	−4.8	−10 to −5
Foliar tissues:		
TNC	27	15 to 75
TNC:protein	33	26 to 125
TNC:minerals	33	24 to 98
protein	−4.8	−19 to −14
minerals	−4.8	−12 to −5

Changes (%) in various plant quality indicators caused by: (1) Adding a teaspoon of TNC (~5g of starch-and-sugars mixture) per 100g of dry mass (DM) of plant tissue, an:d (2) growing plants in twice-ambient CO_2 atmosphere. Changes due to the addition of TNC are calculated assuming:the baseline TNC content of 65% for grains and tubers, and 15% for foliar tissues. The C content is assumed to be ~42% for plant tissues and TNC.
DOI: 10.7554/eLife.02245.013

Stoichiometric thought experiment

A randomized controlled trial for a human diet based exclusively (directly or indirectly) on plants grown in eCO_2 is unlikely and ethically questionable; and even if feasible, the trial might take years to generate results. In lieu of relevant data, we can employ a thought experiment. While such 'experiments' are usually reserved for physical sciences, any living system, notwithstanding its complexity, adheres to simple but irrefutable elemental mass balance, which can help us to elucidate plausible scenarios.

For simplicity, let us focus on one question: how can a 5% reduction in the plant mineral content affect human nutrition? Thus, we ignore other potential or likely CO_2 effects: for example higher agricultural yields; altered concentrations of lipids, vitamins, and polyphenols; substantially higher TNC:protein and TNC:minerals; differential C_3 and C_4 plant responses; changes in the phytate content that affects mineral bioavailability (*Manoj-Kumar, 2011*); and multiplicative health effects of the concomitant declines of many minerals in the same tissue.

Suppose that starting tomorrow and without our knowledge, the baseline mineral content of all plants on Earth drops by 5%. A self-evident but easily overlooked mass-balance law tells us that neither thermal nor mechanical processing of

raw plants enriches them with minerals (i.e., transmutations are impossible). Thus, the mineral decline in raw crops will follow into plant-based foods (except for a few food items that are fortified with certain minerals in some countries).

We can safely assume that the individuals, whose dietary intake of each essential mineral has exceeded the recommended dietary intake (RDI) by >5%, will be unaffected by the depletion. This leaves us with the majority of the human population, whose diet is either at risk of deficiency or already deficient in atleast one mineral (*WHO, 2002*; *Kennedy et al., 2003*; *Stein, 2009*). Though a human body can synthesize complex compounds (e.g., vitamins K and D, non-essential amino acids), the mass balance low implies that *no organism can synthesize any amount of any mineral*. Therefore, to compensate for the mineral deficit, an organism has to increase mineral intake (or, otherwise, endure the consequences of the deficit). Taking supplements or intentionally shifting one's diet toward mineral-rich foods, for example animal products, can eliminate the deficit. Such dietary changes, however, presuppose behavioral adjustments on the part of the individuals who are aware of their mineral deficiency and have both the means and motivation to address it. A simpler way to compensate for the mineral deficit is to *increase food intake*, whether consciously or not. (The notion of compensatory feeding is not entirely alien—herbivores *do* increase consumption by 14–16%, when consuming plants grown in eCO_2; *Stiling and Cornelissen, 2007*; *Robinson et al., 2012*).

For a calorie deficient person, eating 5% more (to be exact 5.26%, because 1.0526*.95 ≈ 1) is likely to be beneficial. However, for a calorie sufficient but mineral deficient person, eating 5% more could be detrimental. The dynamic mathematical model of human metabolism, which links weight changes to dietary and behavioral changes (*Hall et al., 2011*), can help to quantify the effect of a prolonged 5% increase in food intake. When parameterized with anthropometric data for an average moderately active American female (age 38, height 163 cm, weight 76 kg, BMI 28.6, energy intake 2431 kcal/day [10171 kJ]) (*Fryar et al., 2012*; *CIA, 2013*), the model outputs a weight gain of 4.8 kg over a 3-year period, provided all other aspects of behavior and diet remain unchanged. For a male, the respective weight gain is 5.8 kg. The results are congruent with *Hill et al. (2003)*, who argued that a 4–5% difference in total daily energy intake, a mere 100 kcal/day, could be responsible for most weight gain in the population.

The above 'experiment' suggests that a systemic and sustained 5% mineral depletion in plants can be nutritionally significant. While the rise in the atmospheric CO_2 concentration is expected to be nearly uniform around the globe, its impact on crop quality might unequally affect the human population: from no detrimental effects for the well-nourished to potential weight gain for the calorie-sufficient but mineral-undernourished.

Has rising CO_2 already altered the plant ionome?

The rise in CO_2 levels over the last 18–30 years has already been implicated in the two effects that can influence the plant ionome: higher C assimilation and plant growth (*Donohue et al., 2013*), and lower transpiration (*Keenan et al., 2013*). Considering that over the last 250 years, the atmospheric CO_2 concentration has increased by 120 ppm—an increase that is not far from the mean 184 ppm enrichment in the FACE studies—it is plausible that plant quality has changed. Indeed, declines in mineral concentrations have been found in wild plants and in crop fruits, vegetables, and grains over 22–250 years (*Penuelas and Matamala, 1993*; *Duquesnay et al., 2000*; *Davis et al., 2004*; *Ekholm et al., 2007*; *Fan et al., 2008*; *Jonard et al., 2009*). While the mineral declines in crops can be an unintended consequence of the Green Revolution that produced high-yield cultivars with altered mineral content (*Davis et al., 2004*; *Fan et al., 2008*), the reason for the mineral declines in wild plants cannot be attributed to it.

Can eCO_2 directly affect human health? *Hersoug et al. (2012)* proposed that rising CO_2 promotes weight gains and obesity in the human population directly (via breathing) by reducing the pH of blood and, consequently, increasing appetite and energy intake. Weight gain has been observed in wild mammals, lab animals, and humans over the last several decades (*Klimentidis et al., 2011*). However, it is not clear what role, if any, the rising CO_2 could have played either directly (breathing) or indirectly (altered plant quality). And disentangling the rising CO_2 effect from other plausible factors currently does not seem feasible due to scarce data. This brings us to the broader issue of detecting—amid high local noise—signals that are small in their magnitude but global in their scope.

Hidden shifts of global change

While some scientific areas (e.g., genomics, bioinformatics) have experienced a data deluge, many areas of global change, including the issue of shifting plant quality, have been hindered by chronic

data scarcity. Fortunately, researchers worldwide have been steadily generating data on the effects of eCO_2 on the chemical composition of plants. It is their collective efforts that have made it possible to reveal the CO_2-induced shift in the plant ionome.

Human activities profoundly alter the biogeochemical cycle not only of C but also of N, P, and S, which are central to all known life forms. It is plausible that other subtle global shifts in the physiology and functioning of organisms lurk amid highly noisy data. The small magnitude of such shifts makes them hard to detect and easy to dismiss. But by virtue of being global and sustained, the shifts can be biologically potent. Revealing hidden shifts requires plentiful data to attain sufficient statistical power. (For example, *Rohde et al. (2013)* analyzed 14 million *mean* monthly local temperature records to uncover the 1.5°C rise in the global average temperature since 1753—undoubtedly a potent but a very small change relative to the variations of tens of degrees in local temperature.)

New data on the effects of eCO_2 on plant quality (e.g., minerals, TNC: protein, TNC:minerals, lipids, bioavailability of nutrients) can be generated very cost-efficiently by analyzing fresh and archived plant samples collected at FACE centers worldwide (the project leaders of many centers are keen to share such samples; PS Curtis, BA Kimball, R Oren, PB Reich, C Stokes; IL personal communication, July, 2006). With regard to minerals, the application of the high-throughput techniques of ionomics (*Salt et al., 2008*) can generate rich phenotypic data that can be linked with functional genomics. Such analyses will shed more light on changes in plant quality in the rising CO_2 world. Anticipating and assessing such changes will help not only in mitigating their effects but also in steering efforts to breed nutritionally richer crops for the improvement of human health worldwide.

Materials and methods

Search for data

I searched Google Scholar, Google, PubMed, the ISI Web of Science, AGRICOLA, and Scopus to find relevant articles with sensible combinations of two or more of the following search-words: elevated, rising, CO_2, carbon dioxide, ppm, FACE, effects, content, concentration, %, mg, dry matter, micronutrients, plant(s), crop(s), tree(s), C_3, C_4, foliar, leaves, grains, seeds, tubers, fruits, minerals, chemical elements, and names/symbols of various chemical elements (e.g., zinc/Zn). I found additional studies from references in the articles identified in the initial searches.

Study suitability and data selection criteria

Among all plant tissues for which mineral concentrations are reported in the literature, the most abundant data are on foliar tissues (leaves, needles, shoots), and—for herbaceous plants—on above ground parts. Hence, focusing on the foliar tissues and above ground parts allows one to maximize the number of *independent* observations of the effect of eCO_2 on each mineral. Although the data on edible parts of crops are scarcer, a dataset on crop edible tissues was compiled due to their direct relevance for human nutrition.

The following objective and uniform criteria were applied for deciding which studies to include into the dataset: (1) a study grew plants at two or more CO_2 levels, (2) a study directly measured the content of one or more minerals in foliar or edible plant tissues at low (ambient) and high (elevated) CO_2 levels, and (3) a study reported either absolute concentrations at each treatment or relative change/lack thereof in the concentrations for each mineral between treatments. Studies that indirectly deduced mineral concentrations, reported data on N but not on any mineral, exposed only a part (e.g., a branch) of the plant, used super-elevated or uncontrolled CO_2 levels were not included. *Table 3* lists all the studies together with their respective species/cultivars and CO_2 enrichment levels (the dataset with all the details is deposited at Dryad and GitHub). When a study reported the low CO_2 level as 'ambient' with no specific numerical values, then I used the Keeling curve to approximate the ambient CO_2 level for the year the study was carried out.

The following data-inclusion rules were applied to the studies with multiple co-dependent datasets for the foliar dataset: (1) the lowest and the highest CO_2 levels for studies with multiple CO_2 levels, (2) the control and single-factor CO_2 for studies with environmental co-factors (e.g., observations from combined eCO_2 and ozone experiments were excluded), (3) the highest nutrient regime when the control could not be identified in a study with multiple nutrient co-factors, (4) the last point, that is the longest exposure to ambient/eCO_2 for studies with time series, (5) the most mature needles/leaves for studies reporting foliar tissues of various ages. If, in rare instances, a publication reported three

Table 3. Studies covered in the meta-analysis of CO_2 effects on the plant ionome.

Species	Common name	Crop	+CO2	Country	Reference
Acer pseudoplatanus	maple tree	No	260		*Overdieck, 1993*
Acer rubrum	red maple tree	No	200	USA	*Finzi et al., 2001*
Agrostis capillaris	grass	No	340	UK	*Baxter et al., 1994*
Agrostis capillaris	grass	No	250		*Newbery et al., 1995*
Alnus glutinosa	alder tree	No	350	UK	*Temperton et al., 2003*
Alphitonia petriei	rainforest tree	No	440		*Kanowski, 2001*
Ambrosia dumosa	shrub	No	180	USA	*Housman et al., 2012*
Arabidopsis thaliana	thale cress	No	450		*Niu et al., 2013*
Arabidopsis thaliana	thale cress	No	330		*Teng et al., 2006*
Betula pendula 'Roth'	birch tree	No	349	Finland	*Oksanen et al., 2005*
Bouteloua curtipendula	grass	No	230		*Polley et al., 2011*
Bromus tectorum	cheatgrass	No	150		*Blank et al., 2006*
Bromus tectorum	cheatgrass	No	150		*Blank et al., 2011*
Calluna vulgaris	heather shrub	No	200		*Woodin et al., 1992*
Cercis canadensis	red bud tree	No	200	USA	*Finzi et al., 2001*
Chrysanthemum morifolium	chrysanth	No	325		*Kuehny et al., 1991*
Cornus florida	dogwood tree	No	200	USA	*Finzi et al., 2001*
Fagus sylvatica	beech tree	No	260		*Overdieck, 1993*
Fagus sylvatica	beech tree	No	300		*Rodenkirchen et al., 2009*
Festuca pratensis	meadow fescue	No	320		*Overdieck, 1993*
Festuca vivipara	grass	No	340	UK	*Baxter et al., 1994*
Flindersia brayleyana	rainforest tree	No	440		*Kanowski, 2001*
Galactia elliottii	Elliott's milkpea	No	325	USA	*Hungate et al., 2004*
Larix kaempferi	larch tree	No	335	Japan	*Shinano et al., 2007*
Lepidium latifolium	peppergrass	No	339		*Blank and Derner, 2004*
Liquidambar styraciflua	sweetgum tree	No	200	USA	*Finzi et al., 2001*
Liquidambar styraciflua	sweetgum tree	No	167	USA	*Johnson et al., 2004*
Liquidambar styraciflua	sweetgum tree	No	156–200	USA	*Natali et al., 2009*
Liriodendron tulipifera	tulip tree	No	325		*O'Neill et al., 1987*
Lolium perenne	grass	No	320		*Overdieck, 1993*
Lolium perenne	grass	No	290	Germany	*Schenk et al., 1997*
Lupinus albus	white lupin	No	550		*Campbell and Sage, 2002*
Lycium pallidum	shrub	No	180	USA	*Housman et al., 2012*
Nephrolepis exaltata	fern	No	650		*Nowak et al., 2002*
Pelargonium x hortorum 'Maverick White'	geranium	No	330		*Mishra et al., 2011*
Picea abies 'Karst.'	spruce tree	No	350		*Pfirrmann et al., 1996*
Picea abies 'Karst.'	spruce tree	No	300		*Rodenkirchen et al., 2009*
Picea abies 'Karst.'	spruce tree	No	300		*Weigt et al., 2011*
Picea rubens	spruce tree	No	350		*Shipley et al., 1992*
Pinus ponderosa	pine tree	No	346	USA	*Walker et al., 2000*
Pinus ponderosa 'Laws.'	pine tree	No	350	USA	*Johnson et al., 1997*
Pinus sylvestris	pine tree	No	331		*Luomala et al., 2005*

Table 3. Continued on next page

Table 3. Continued

Species	Common name	Crop	+CO2	Country	Reference
Pinus sylvestris	pine tree	No	225	Finland	*Utriainen et al., 2000*
Pinus taeda	loblolly pine tree	No	200	USA	*Finzi et al., 2001*
Pinus taeda	pine tree	No	200	USA	*Natali et al., 2009*
Poa alpina	grass	No	340	UK	*Baxter et al., 1994*
Poa alpina	grass	No	340	UK	*Baxter et al., 1997*
Pteridium aquilinum	fern	No	320		*Zheng et al., 2008*
Pteridium revolutum	fern	No	320		*Zheng et al., 2008*
Pteris vittata	fern	No	320		*Zheng et al., 2008*
Quercus chapmanii	oak tree	No	350	USA	*Natali et al., 2009*
Quercus geminata	oak tree	No	350	USA	*Johnson et al., 2003*
Quercus geminata	oak tree	No	350	USA	*Natali et al., 2009*
Quercus myrtifolia	oak tree	No	350	USA	*Johnson et al., 2003*
Quercus myrtifolia	oak tree	No	350	USA	*Natali et al., 2009*
Quercus suber	cork oak tree	No	350		*Niinemets et al., 1999*
Schizachyrium scoparium	grass	No	230		*Polley et al., 2011*
Sorghastrum nutans	grass	No	230		*Polley et al., 2011*
Sporobolus kentrophyllus	grass	No	330		*Wilsey et al., 1994*
Trifolium alexandrinum 'Pusa Jayant'	berseem clover	No	250	India	*Pal et al., 2004*
Trifolium pratense	red clover	No	320		*Overdieck, 1993*
Trifolium repens	white clover	No	320		*Overdieck, 1993*
Trifolium repens	white clover	No	290	Germany	*Schenk et al., 1997*
Trifolium repens	white clover	No	615		*Tian et al., 2014*
Trifolium repens 'Regal'	white clover	No	330		*Heagle et al., 1993*
Vallisneria spinulosa	macrophyte	No	610		*Yan et al., 2006*
Apium graveolens	celery	Yes	670		*Tremblay et al., 1988*
Brassica juncea 'Czern'	mustard	Yes	500	India	*Singh et al., 2013*
Brassica napus 'Qinyou 8'	rapeseed	Yes	615		*Tian et al., 2014*
Brassica napus 'Rongyou 10'	rapeseed	Yes	615		*Tian et al., 2014*
Brassica napus 'Zhongyouza 12'	rapeseed	Yes	615		*Tian et al., 2014*
Brassica napus 'Campino'	oilseed rape	Yes	106	Germany	*Högy et al., 2010*
Brassica rapa 'Grabe'	turnip	Yes	600		*Azam et al., 2013*
Citrus aurantium	orange tree	Yes	300	USA	*Penuelas et al., 1997*
Citrus madurensis	citrus tree	Yes	600		*Keutgen and Chen, 2001*
Cucumis sativus	cucumber	Yes	650		*Peet et al., 1986*
Daucus carota 'T-1-111'	carrot	Yes	600		*Azam et al., 2013*
Fragaria x ananassa	strawberry	Yes	600		*Keutgen et al., 1997*
Glycine max 'Merr.'	soybean	Yes	360	USA	*Prior et al., 2008*
Glycine max 'Merr.'	soybean	Yes	200		*Rodriguez et al., 2011*
Gossypium hirsutum 'Deltapine 77'	cotton	Yes	180	USA	*Huluka et al., 1994*
Hordeum vulgare	barley	Yes	175	Germany	*Erbs et al., 2010*
Hordeum vulgare 'Alexis'	barley	Yes	334	Germany	*Manderscheid et al., 1995*

Table 3. Continued on next page

Table 3. Continued

Species	Common name	Crop	+CO2	Country	Reference
Hordeum vulgare 'Arena'	barley	Yes	334	Germany	*Manderscheid et al., 1995*
Hordeum vulgare 'Europa'	barley	Yes	400		*Haase et al., 2008*
Hordeum vulgare 'Iranis'	barley	Yes	350		*Pérez-López et al., 2014*
Hordeum vulgare 'Theresa'	barley	Yes	170	Germany	*Wroblewitz et al., 2013*
Lactuca sativa 'BRM'	lettuce	Yes	308		*Baslam et al., 2012*
Lactuca sativa 'Mantilla'	lettuce	Yes	350		*Chagvardieff et al., 1994*
Lactuca sativa 'MV'	lettuce	Yes	308		*Baslam et al., 2012*
Lactuca sativa 'Waldmann's Green'	lettuce	Yes	600		*McKeehen et al., 1996*
Lycopersicon esculentum 'Astra'	tomato	Yes	600		*Khan et al., 2013*
Lycopersicon esculentum 'Eureka'	tomato	Yes	600		*Khan et al., 2013*
Lycopersicon esculentum 'Mill.'	tomato	Yes	360		*Li et al., 2007*
Lycopersicon esculentum 'Zheza 809'	tomato	Yes	450		*Jin et al., 2009*
Mangifera indica 'Kensington'	mango tree	Yes	350		*Schaffer and Whiley, 1997*
Mangifera indica 'Tommy Atkins'	mango tree	Yes	350		*Schaffer and Whiley, 1997*
Medicago sativa	alfalfa	Yes	615		*Tian et al., 2014*
Medicago sativa 'Victor'	alfalfa	Yes	100	UK	*Al-Rawahy et al., 2013*
Oryza sativa	rice	Yes	200	China	*Pang et al., 2005*
Oryza sativa 'Akitakomachi'	rice	Yes	205–260	Japan	*Lieffering et al., 2004*
Oryza sativa 'Akitakomachi'	rice	Yes	250	Japan	*Yamakawa et al., 2004*
Oryza sativa 'BRRIdhan 39'	rice	Yes	210	Bangladesh	*Razzaque et al., 2009*
Oryza sativa 'Gui Nnong Zhan'	rice	Yes	500		*Li et al., 2010*
Oryza sativa 'IR 72'	rice	Yes	296	Philippines	*Ziska et al., 1997*
Oryza sativa 'Japonica'	rice	Yes	200	China	*Jia et al., 2007*
Oryza sativa 'Jarrah'	rice	Yes	350		*Seneweera and Conroy, 1997*
Oryza sativa 'Khaskani'	rice	Yes	210	Bangladesh	*Razzaque et al., 2009*
Oryza sativa 'Rong You 398'	rice	Yes	500		*Li et al., 2010*
Oryza sativa 'Shakkorkhora'	rice	Yes	210	Bangladesh	*Razzaque et al., 2009*
Oryza sativa 'Shan You 428'	rice	Yes	500		*Li et al., 2010*
Oryza sativa 'Tian You 390'	rice	Yes	500		*Li et al., 2010*
Oryza sativa 'Wu Xiang jing'	rice	Yes	200	China	*Guo et al., 2011*
Oryza sativa 'Wuxiangjing 14'	rice	Yes	200	China	*Ma et al., 2007*
Oryza sativa 'Wuxiangjing 14'	rice	Yes	200	China	*Yang et al., 2007*
Oryza sativa 'Yin Jing Ruan Zhan'	rice	Yes	500		*Li et al., 2010*
Oryza sativa 'Yue Za 889'	rice	Yes	500		*Li et al., 2010*
Phaseolus vulgaris 'Contender'	bean	Yes	340		*Mjwara et al., 1996*
Phaseolus vulgaris 'Seafarer'	bean	Yes	870		*Porter and Grodzinski, 1984*
Raphanus sativus 'Mino'	radish	Yes	600		*Azam et al., 2013*
Raphanus sativus 'Cherry Belle'	radish	Yes	380		*Barnes and Pfirrmann, 1992*
Raphanus sativus 'Giant White Globe'	radish	Yes	600		*McKeehen et al., 1996*
Rumex patientia x R. Tianschanicus 'Rumex K-1'	buckwheat	Yes	615		*Tian et al., 2014*

Table 3. Continued on next page

Table 3. Continued

Species	Common name	Crop	+CO2	Country	Reference
Secale cereale 'Wintergrazer-70'	rye	Yes	615		*Tian et al., 2014*
Solanum lycopersicum '76R MYC+'	tomato	Yes	590		*Cavagnaro et al., 2007*
Solanum lycopersicum 'rmc'	tomato	Yes	590		*Cavagnaro et al., 2007*
Solanum tuberosum	potato	Yes	500		*Cao and Tibbitts, 1997*
Solanum tuberosum 'Bintje'	potato	Yes	170	Germany	*Högy and Fangmeier, 2009*
Solanum tuberosum 'Bintje'	potato	Yes	278-281	Sweden	*Piikki et al., 2007*
Solanum tuberosum 'Bintje'	potato	Yes	305-320	Europe	*Fangmeier et al., 2002*
Solanum tuberosum 'Dark Red Norland'	potato	Yes	345	USA	*Heagle et al., 2003*
Solanum tuberosum 'Superior'	potato	Yes	345	USA	*Heagle et al., 2003*
Sorghum bicolor	sorghum	Yes	360	USA	*Prior et al., 2008*
Spinacia oleracea	spinach	Yes	250	India	*Jain et al., 2007*
Trigonella foenum-graecum	fenugreek	Yes	250	India	*Jain et al., 2007*
Triticum aestivum	wheat	Yes	175	Germany	*Erbs et al., 2010*
Triticum aestivum 'Ningmai 9'	wheat	Yes	200	China	*Ma et al., 2007*
Triticum aestivum 'Triso'	wheat	Yes	150	Germany	*Högy et al., 2009*
Triticum aestivum 'Triso'	wheat	Yes	150	Germany	*Högy et al., 2013*
Triticum aestivum 'Alcazar'	wheat	Yes	350		*de la Puente et al., 2000*
Triticum aestivum 'Batis'	wheat	Yes	170	Germany	*Wroblewitz et al., 2013*
Triticum aestivum 'Dragon'	wheat	Yes	305-320	Sweden	*Pleijel and Danielsson, 2009*
Triticum aestivum 'HD-2285'	wheat	Yes	250	India	*Pal et al., 2003*
Triticum aestivum 'Janz'	wheat	Yes	166	Australia	*Fernando et al., 2014*
Triticum aestivum 'Jinnong 4'	wheat	Yes	615		*Tian et al., 2014*
Triticum aestivum 'Minaret'	wheat	Yes	278	Germany	*Fangmeier et al., 1997*
Triticum aestivum 'Minaret'	wheat	Yes	300	Europe	*Fangmeier et al., 1999*
Triticum aestivum 'Rinconada'	wheat	Yes	350		*de la Puente et al., 2000*
Triticum aestivum 'Star'	wheat	Yes	334	Germany	*Manderscheid et al., 1995*
Triticum aestivum 'Turbo'	wheat	Yes	334	Germany	*Manderscheid et al., 1995*
Triticum aestivum 'Turbo'	wheat	Yes	350		*Wu et al., 2004*
Triticum aestivum 'Veery 10'	wheat	Yes	410		*Carlisle et al., 2012*
Triticum aestivum 'Yangmai'	wheat	Yes	200	China	*Guo et al., 2011*
Triticum aestivum 'Yitpi'	wheat	Yes	166	Australia	*Fernando et al., 2012a*
Triticum aestivum 'Yitpi'	wheat	Yes	166	Australia	*Fernando et al., 2012b*
Triticum aestivum 'Yitpi'	wheat	Yes	166	Australia	*Fernando et al., 2012c*
Triticum aestivum 'Yitpi'	wheat	Yes	166	Australia	*Fernando et al., 2014*

The table provides species name, common name, the type of experimental set up, the level of CO_2 enrichment, and indicates whether the species is a crop. Countries are listed only for FACE and OTC type experiments with 'Europe' accounting for combined data from Belgium, Denmark, Finland, Germany, Sweden, and the UK.

or more separate datasets for the same species or cultivar, the data were averaged prior to the inclusion into the foliar dataset. For the edible tissue dataset, the study inclusion rules were the same as for the foliar dataset with the following exception: due to relative scarcity of data for edible tissues, the data with co-factors were included in the dataset (e.g., observations from combined eCO_2 and ozone experiments were included). The 'Additional info' column in the dataset specifies exactly what datasets were extracted from each study with multiple datasets.

The above publication-inclusion and data-inclusion rules allow treating each study as independent in the dataset. At no instance, potentially co-dependent observations (e.g., multiple observations of the same plant throughout a growing season or observations of various parts of the same plant) were included in either the foliar or the edible dataset as separate studies. I used GraphClick v.3.0 and PixelStick v.2.5 to digitize data presented in a graphical form, for example bar charts.

The foliar dataset covers 4733 observations of 25 chemical elements in 110 species and cultivars. The edible tissues dataset covers 3028 observations of 23 elements in 41 species and cultivars. The FACE studies cover 2264 observations of 24 elements in 25 species and cultivars. The two datasets reflect data on 125 C_3 and 5 C_4 species/cultivars.

Effect size measure

While the amount of statistical details provided in each study varies considerably, the following data were extractable from each study: (1) the relative change (or lack thereof) in the mean concentration between the low and the high CO_2 treatments: *(E-A)/A*, where *A* and *E* are the mean concentrations of an element at the low and the high CO_2 treatments respectively, (2) the sample size or the number of replicates (*n*).

Since a decrease in the concentration of a mineral is limited to 100%, but an increase in its concentration is theoretically unlimited, a standard technique was applied to reduce biases towards increases. Specifically, the natural log of the response ratio, that is *ln(E/A)*, was used as the effect size metric (e.g., *Hedges et al., 1999*; *Jablonski et al., 2002*; *Taub et al., 2008*). The response ratio, *r = E/A*, was calculated from the relative change as follows: *r = 1+(E-A)/A*. After performing statistical analyses, I converted all the results back from the log form to report them as ordinary percent changes.

Making results replicable

Published meta-analytic and biostatistical results need to be replicable and reproducible, and the process of replication needs to be made as easy as possible and clearly traceable to the original sources (*Peng, 2009*). In this regard, I have made the following efforts to ease the replication (from the original sources) of each and every result presented here:

1. While copyright restrictions do not permit posting the original published data sources online, I will share, upon request, all the data sources in PDF form, where all the pertinent data are clearly marked for easy identification, thus removing any potential ambiguity about what data were extracted from each study.
2. The entire dataset for the foliar and the edible tissues is available at Dryad digital depository, www.datadryad.org, under 10.5061/dryad.6356f. The dataset is available as an Excel file (formatted for easy viewing) and as a 'CSV' file; the latter is made-ready (tidy) for analysis with open-source (*R Core Team, 2014*) and commercial statistical packages (e.g., SPSS).
3. An executable R code to generate individual results is available with the dataset at the above-mentioned depository and at GitHub: https://github.com/loladze/co2. Assistance for replicating any result and figure presented in this study will be provided to any interested party.

Statistical analysis

I performed all the analyses using R (*R Core Team, 2014*), SPSS v. 21 (IBM, Armonk, NY, USA) and G*Power 3 (*Faul et al., 2007*). Meta-analytic studies often weight effect sizes by the reciprocal of their variance, which tends to give a greater weight to studies with greater precision. However, many eCO_2 studies do not report measures of variation in the data (standard error, standard deviation, or variance). In lieu of the measures of variance, studies can be weighted by the number of replicates (*n*) or, alternatively, each study can be assigned equal weight, that is, unweighted method (*Jablonski et al., 2002*). I used both methods (weighted and unweighted) to calculate the means of effect sizes with 95% CIs and compared the results of both methods. Nearly in all instances, the difference between the weighted and the unweighted means was small and lesser than the standard error of the unweighted mean. For example, across all the FACE studies, the overall mineral change was −6.1% (−7.8 to −4.4) when unweighted cf. the −6.5% (−8.0 to −5.1) when weighted. For the reason of close similarity between weighted and unweighted approaches, I used the simpler out of the two methods, that is the unweighted one, when reporting the results.

Since the distribution of effect sizes is not necessarily normal, I applied both parametric (*t* test) and non-parametric (bootstrapping with 10,000 replacements) tests for calculating the 95% CI for the

mean effect size and the statistical power. The latter was calculated for: (1) an absolute effect size of 5%, and (2) the probability of Type I error, $\alpha = 0.05$. If the variance of a small sample << the true population variance, then this leads to substantial overestimations of Cohen's d and the statistical power. To be conservative when estimating power for small samples (m <20), I used the *larger* of the sample standard deviation or 0.21, which is the standard deviation for the entire mineral dataset.

The results from the parametric and non-parametric tests were very close. For example, for Zn in edible tissues (sample size = 65), t test yields (−11.4%, −14.0 to −8.7) and 0.91 power cf. (−11.4%, −13.9 to −8.7) and 0.92 power for the bootstrapping procedure. A close similarity between the results of t test and non-parametric test is expected when sample size (m, the number of independent observations for each mineral) is >30, which often was the case in this study. For reporting purposes, I used the 95% CI and the power generated by the non-parametric method, that is, the bootstrapping procedure.

Testing for publication bias

To test for publication bias or 'the file drawer effect' in the dataset, I plotted effect sizes against corresponding sample sizes/replicates, n, to provide a simple visual evaluation of the distribution of effect sizes (*Figure 9*). The resulting cloud of points is funnel-shaped, narrowing toward larger sample sizes, and overall is symmetrical along the mean effect size. This indicates the absence of any significant publication bias (*Egger et al., 1997*).

Fragmenting the dataset into categories

Meta-analytic CO_2 studies often partition their datasets into various categories (e.g., plant group, plant tissue, fertilization, or water regime) to estimate effect sizes for each category. Such data fragmentation, however, is warranted only if the statistical power of the resulting test for each category is adequate. Otherwise, low power can lead to non-significant outcomes and Type II errors. As tempting as it can be to partition the current dataset into many categories and cases (e.g., Zn in fruits, Fe in tuber, Cu in annuals, multiple CO_2 levels), only by fragmenting the data into sufficiently large categories an adequate statistical power can be retained. Such categories include: foliar tissues, edible tissues, woody plants (trees and shrubs), herbaceous plants, FACE studies, non-FACE studies, crops, wild plants (all non-crops, including ornamental plants), C_3 plants, C_4 plants, rice, wheat, barley, and potato. Furthermore, I fragmented the data for C_3 plants, the foliar and the edible tissues, the non-FACE and the FACE studies into individual chemical elements and into individual common plant names (e.g., all rice cultivars grouped under 'rice'). For the regional analysis, I used only OTC and FACE studies because they reflect local environment much more accurately than studies using complete-enclosures (e.g., closed chamber, glasshouse). If an OTC or FACE study did not report precise geographic coordinates, then the latitude and longitude of a nearby research facility or city was used (all coordinates in the dataset are in decimal units). *Figures 1–7* include results with the statistical power >0.40 for each element, country, region, plant tissue or category. Generally, power >0.80 is considered acceptable (*Cohen, 1988*). Unfortunately, such a level was achievable only for elements for which the data are most abundant and for the ionomes of some plant groups and species. Note that the power was calculated for a 5% effect size, while the true effect size is likely to be larger (~8%); therefore, the true power is likely to be higher than the calculated power for most results. All the results, irrespective of the statistical power, can be found in *Figure 1–source data 1*. Furthermore, *Figure 1* shows the mean effect sizes (with their 95% CI) plotted against their respective statistical powers for all the minerals and all the plant groups/tissues.

Formula for calculating percentage changes in TNC:protein and TNC:minerals

If the concentration of substance X in a plant increases by x% and concomitantly the concentration of substance Y decreases by y% in the plant, then the X-to-Y ratio of the plant (X:Y) increases by:

$$\frac{x+y}{100-y} \cdot 100\% \tag{1}$$

Proof

Let us denote the initial concentrations of substances X and Y in a plant as x_A and y_A, respectively. Suppose the X and Y contents in the plant changed by x% and $-y$%, respectively. Then the new X content in the plant, x_E, is

$$x_E = x_A \cdot (100 + x)\,\%,$$

and the new Y content in the plant, y_E, is

$$y_E = y_A \cdot (100 - y)\,\%.$$

The original $X : Y = x_A/y_A$, while the new $X : Y = x_E/y_E$. Since the percentage change in the $X{:}Y$ equals to:

$$\frac{new - original}{original} \cdot 100\% = \left(\frac{new}{original} - 1\right) \cdot 100\%,$$

substituting x_A/y_A and x_E/y_E for the original and the new, respectively, yields:

$$\frac{x_E/y_E}{x_A/y_A} - 1 = \frac{x_E \cdot y_E}{x_A \cdot y_A} - 1 = \frac{(x_A\,(100 + x)\,\%) \cdot y_A}{x_A\,(y_A\,(100 - y)\,\%)} - 1 = \frac{100 + x}{100 - y} - 1 = \frac{x + y}{100 - y}.$$

An advantage of *Equation 1* is that it holds true irrespective of whether the decrease in Y is driven by some reason applicable only to Y or by the increase in X, that is the dilution by X.

Acknowledgements

Additional information

Funding

Funder	Author

Author contributions

IL, Conception and design, Acquisition of data, Analysis and interpretation of data, Drafting or revising the article

Additional files

Major dataset

The following dataset was generated:

Author(s)	Year	Dataset title	Dataset ID and/or URL	Database, license, and accessibility information
Loladze I	2014	CO_2 Dataset (CSV format); CO_2 Dataset (XLSX format); R Code for the CO_2 dataset	http://dx.doi.org/10.5061/dryad.6356f	Available at Dryad Digital Repository under a CC0 Public Domain Dedication.

References

AAAC Climate Science Panel. 2014. What we know: the reality, risks and response to climate change. URL http://whatweknow.aaas.org

Al-Rawahy SH, Sulaiman H, Farooq Sa, Karam MF, Sherwani N. 2013. Effect of O3 and CO2 levels on growth, biochemical and nutrient parameters of alfalfa (*Medicago Sativa*). *APCBEE Procedia* **5**:288–295. doi: 10.1016/j.apcbee.2013.05.050.

Arnaud J, Bertrais S, Roussel AM, Arnault N, Ruffieux D, Favier A, Berthelin S, Estaquio C, Galan P, Czernichow S, Hercberg S. 2007. Serum selenium determinants in French adults: the SU.VI.M.AX study. *British Journal of Nutrition* **95**:313–320. doi: 10.1079/BJN20051528.

Azam A, Khan I, Mahmood A. 2013. Yield, chemical composition and nutritional quality responses of carrot, radish and turnip to elevated atmospheric carbon dioxide. *Journal of the Science of Food and Agriculture* **93**:3237–3244. doi: 10.1002/jsfa.6165.

Barnes J, Pfirrmann T. 1992. The influence of CO2 and O3, singly and in combination, on gas exchange, growth and nutrient status of radish. *New Phytologist* **121**:403–412. doi: 10.1111/j.1469-8137.1992.tb02940.x.

Baslam M, Garmendia I, Goicoechea N. 2012. Elevated CO2 may impair the beneficial effect of arbuscular mycorrhizal fungi on the mineral and phytochemical quality of lettuce. *Annals of Applied Biology* **161**:180–191. doi: 10.1111/j.1744-7348.2012.00563.x.

Baxter R, Ashenden TW, Farrar JF. 1997. Effect of elevated CO2 and nutrient status on growth, dry matter partitioning and nutrient content of *Poa alpina* var. *vivipara* L. *Journal of Experimental Botany* **48**:1477–1486. doi: 10.1093/jxb/48.7.1477.

Baxter R, Gantley M, Ashenden TW, Farrar JF. 1994. Effects of elevated carbon dioxide on three grass species from montane pasture II. Nutrient uptake, allocation and efficiency of use. *Journal of Experimental Botany* **45**:1267–1278. doi: 10.1093/jxb/45.9.1267.

Blank R, Morgan T, Ziska L, White R. 2011. Effect of atmospheric CO2 levels on nutrients in cheatgrass tissue. *Natural Resources and Environmental Issues* **16**:1–5.

Blank RR, Derner JD. 2004. Effects of CO2 enrichment on plant-soil relationships of *Lepidium latifolium*. *Plant and Soil* **262**:159–167. doi: 10.1023/B:PLSO.0000037032.43098.5c.

Blank RR, White RH, Ziska LH. 2006. Combustion properties of *Bromus tectorum* L.: influence of ecotype and growth under four CO2 concentrations. *International Journal of Wildland Fire* **15**:227–236. doi: 10.1071/WF05055.

Bloom AJ, Burger M, Rubio Asensio JS, Cousins AB. 2010. Carbon dioxide enrichment inhibits nitrate assimilation in wheat and *Arabidopsis*. *Science* **328**:899–903. doi: 10.1126/science.1186440.

Bouis HE, Welch RM. 2010. Biofortification – a sustainable agricultural strategy for reducing micronutrient malnutrition in the global South. *Crop Science* **50**(Suppl 1):S–20–S–32. doi: 10.2135/cropsci2009.09.0531.

Brown KH, Wuehler SE, Peerson JM. 2001. The importance of zinc in human nutrition and estimation of the global prevalence of zinc deficiency. *Food and Nutrition Bulletin* **22**:113–125.

Button KS, Ioannidis JP, Mokrysz C, Nosek BA, Flint J, Robinson ES, Munafò MR. 2013. Power failure: why small sample size undermines the reliability of neuroscience. *Nature Reviews Neuroscience* **14**:365–376. doi: 10.1038/nrn3475.

Campbell CD, Sage RF. 2002. Interactions between atmospheric CO2 concentration and phosphorus nutrition on the formation of proteoid roots in white lupin (*Lupinus albus* L.). *Plant, Cell & Environment* **25**:1051–1059. doi: 10.1046/j.1365-3040.2002.00883.x.

Cao W, Tibbitts TW. 1997. Starch concentration and impact on specific leaf weight and element concentrations in potato leaves under varied carbon dioxide and temperature. *Journal of Plant Nutrition* **20**:871–881. doi: 10.1080/01904169709365302.

Carlisle E, Myers S, Raboy V, Bloom A. 2012. The effects of inorganic nitrogen form and CO2 concentration on wheat yield and nutrient accumulation and distribution. *Frontiers in Plant Science* **3**:195. doi: 10.3389/fpls.2012.00195.

Cavagnaro TR, Sokolow SK, Jackson LE. 2007. Mycorrhizal effects on growth and nutrition of tomato under elevated atmospheric carbon dioxide. *Functional Plant Biology* **34**:730–736. doi: 10.1071/FP06340.

Chagvardieff P, D'Aletto T, Andre M. 1994. Specific effects of irradiance and CO2 concentration doublings on productivity and mineral content in lettuce. *Advances in Space Research* **14**:269–275. doi: 10.1016/0273-1177(94)90307-7.

CIA. 2013. The World Factbook. Central Intelligence Agency. URL https://www.cia.gov/library/publications/the-world-factbook/

Cohen J. 1988. *Statistical power analysis for the behavioral sciencies*. Hillsdale, NJ: Erlbaum. 2nd edition.

Cotrufo MF, Ineson P, Scott A. 1998. Elevated CO2 reduces the nitrogen concentration of plant tissues. *Global Change Biology* **4**:43–54. doi: 10.1046/j.1365-2486.1998.00101.x.

Davis DR, Epp MD, Riordan HD. 2004. Changes in USDA food composition data for 43 garden crops, 1950 to 1999. *Journal of the American College of Nutrition* **23**:669–682. doi: 10.1080/07315724.2004.10719409.

de la Puente LS, Perez PP, Martinez-Carrasco R, Morcuende RM, del Molino IMM. 2000. Action of elevated CO2 and high temperatures on the mineral chemical composition of two varieties of wheat. *Agrochimica* **44**:221–230.

Donohue RJ, Roderick ML, McVicar TR, Farquhar GD. 2013. Impact of CO2 fertilization on maximum foliage cover across the globe's warm, arid environments. *Geophysical Research Letters* **40**:3031–3035. doi: 10.1002/grl.50563.

Drake BG, Gonzalez-Meler Ma, Long SP. 1997. More efficient plants: a consequence of rising atmospheric CO2? *Annual Review of Plant Physiology and Plant Molecular Biology* **48**:609–639. doi: 10.1146/annurev.arplant.48.1.609.

Duquesnay A, Dupouey JL, Clement A, Ulrich E, Le Tacon F. 2000. Spatial and temporal variability of foliar mineral concentration in beech (*Fagus sylvatica*) stands in northeastern France. *Tree Physiology* **20**:13–22. doi: 10.1093/treephys/20.1.13.

Duval BD, Blankinship JC, Dijkstra P, Hungate BA. 2011. CO2 effects on plant nutrient concentration depend on plant functional group and available nitrogen: a meta-analysis. *Plant Ecology* **213**:505–521. doi: 10.1007/s11258-011-9998-8.

Ebbeling CB, Swain JF, Feldman HA, Wong WW, Hachey DL, Garcia-Lago E, Ludwig DS. 2012. Effects of dietary composition on energy expenditure during weight-loss maintenance. *The Journal of the American Medical Association* **307**:2627–2634. doi: 10.1001/jama.2012.6607.

Egger M, Smith GD, Schneider M, Minder C. 1997. Bias in meta-analysis detected by a simple, graphical test. *British Medical Journal* **315**:629–634. doi: 10.1136/bmj.315.7109.629.

Ekholm P, Reinivuo H, Mattila P, Pakkala H, Koponen J, Happonen A, Hellström J, Ovaskainen M-L. 2007. Changes in the mineral and trace element contents of cereals, fruits and vegetables in Finland. *Journal of Food Composition and Analysis* **20**:487–495. doi: 10.1016/j.jfca.2007.02.007.

Erbs M, Manderscheid R, Jansen G, Seddig S, Pacholski A, Weigel H. 2010. Effects of free-air CO_2 enrichment and nitrogen supply on grain quality parameters and elemental composition of wheat and barley grown in a crop rotation. *Agriculture, Ecosystems & Environment* **136**:59–68. doi: 10.1016/j.agee.2009.11.009.

Fan M-S, Zhao F-J, Fairweather-tait SJ, Poulton PR, Dunham SJ, Mcgrath SP. 2008. Evidence of decreasing mineral density in wheat grain over the last 160 years. *Journal of Trace Elements in Medicine and Biology* **22**:315–324. doi: 10.1016/j.jtemb.2008.07.002.

Fangmeier A, De Temmerman L, Black C, Persson K, Vorne V. 2002. Effects of elevated CO_2 and/or ozone on nutrient concentrations and nutrient uptake of potatoes. *European Journal of Agronomy* **17**:353–368. doi: 10.1016/S1161-0301(02)00071-0.

Fangmeier A, De Temmerman L, Mortensen L, Kemp K, Burke J, Mitchell R, van Oijen M, Weigel H-J. 1999. Effects on nutrients and on grain quality in spring wheat crops grown under elevated CO_2 concentrations and stress conditions in the European, multiple-site experiment "ESPACE-wheat". *European Journal of Agronomy* **10**:215–229. doi: 10.1016/S1161-0301(99)00012-X.

Fangmeier A, Grüters U, Högy P, Vermehren B, Jäger H-J. 1997. Effects of elevated CO_2, nitrogen supply and tropospheric ozone on spring wheat—II. Nutrients (N, P, K, S, Ca, Mg, Fe, Mn, Zn). *Environmental Pollution* **96**:43–59. doi: 10.1016/S0269-7491(97)00013-4.

FAO. 2013. Food and Agriculture Organization of the United Nations, FAOSTAT database. Rome: Food and Agriculture Organization of the United Nations. URL http://faostat.fao.org/

Faul F, Erdfelder E, Lang A-G, Buchner A. 2007. G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods* **39**:175–191. doi: 10.3758/BF03193146.

Fernando N, Panozzo J, Tausz M, Norton RM, Fitzgerald GJ, Myers S, Walker C, Stangoulis J, Seneweera S. 2012c. Wheat grain quality under increasing atmospheric CO_2 concentrations in a semi-arid cropping system. *Journal of Cereal Science* **56**:684–690. doi: 10.1016/j.jcs.2012.07.010.

Fernando N, Panozzo J, Tausz M, Norton R, Fitzgerald G, Seneweera S. 2012a. Rising atmospheric CO_2 concentration affects mineral nutrient and protein concentration of wheat grain. *Food Chemistry* **133**:1307–1311. doi: 10.1016/j.foodchem.2012.01.105.

Fernando N, Panozzo J, Tausz M, Norton RM, Fitzgerald G, Seneweera S. 2012b. Elevated atmospheric CO_2 affects grain sulfur concentration and grain nitrogen/sulfur ratio of wheat (Triticum aestivum L.). In: De Kok LJ, Tabe L, Tausz M, Hawkesford MJ, Hoefgen R, McManus MT, Schnug E, (Eds), *Metabolism in Plants*. Dordrecht, Netherlands: Sp(ringer. p. 231–236. doi: 10.1007/978-94-007-4450-9_28.

Fernando N, Panozzo J, Tausz M, Norton RM, Neumann N, Fitzgerald GJ, Seneweera S. 2014. Elevated CO_2 alters grain quality of two bread wheat cultivars grown under different environmental conditions. *Agriculture, Ecosystems & Environment* **185**:24–33. doi: 10.1016/j.agee.2013.11.023.

Finzi AC, Allen AS, DeLucia EH, Ellsworth DS, Schlesinger WH. 2001. Forest litter production, chemistry, and decomposition following two years of free-air CO_2 enrichment. *Ecology* **82**:470–484. doi: 10.1890/0012-9658(2001)082[0470:FLPCAD]2.0.CO;2.

Fryar CD, Gu Q, Ogden CL. 2012. Anthropometric reference data for children and adults: United States, 2007–2010. *National Center for Health Statistics Vital and Health Statistics* **11**:1–40.

García OP, Long KZ, Rosado JL. 2009. Impact of micronutrient deficiencies on obesity. *Nutrition Reviews* **67**:559–572. doi: 10.1111/j.1753-4887.2009.00228.x.

Guo H, Zhu J, Zhou H, Sun Y, Yin Y, Pei D, Ji R, Wu J, Wang X. 2011. Elevated CO_2 levels affects the concentrations of copper and cadmium in crops grown in soil contaminated with heavy metals under fully open-air field conditions. *Environmental Science & Technology* **45**:6997–7003. doi: 10.1021/es2001584.

Haase S, Rothe A, Kania A, Wasaki J, Römheld V, Engels C, Kandeler E, Neumann G. 2008. Responses to iron limitation in Hordeum vulgare L. as affected by the atmospheric CO_2 concentration. *Journal of Environmental Quality* **37**:1254–1262. doi: 10.2134/jeq2006.0136.

Hall KD, Sacks G, Chandramohan D, Chow CC, Wang YC, Gortmaker SL, Swinburn BA. 2011. Quantification of the effect of energy imbalance on bodyweight. *Lancet* **378**:826–837. doi: 10.1016/S0140-6736(11)60812-X.

Heagle AS, Miller JE, Pursley WA. 2003. Growth and yield responses of potato to mixtures of carbon dioxide and ozone. *Journal of Environment Quality* **32**:1603–1610. doi: 10.2134/jeq2003.1603.

Heagle AS, Miller JE, Sherrill DE, Rawlings JO. 1993. Effects of ozone and carbon dioxide mixtures on two clones of white clover. *New Phytologist* **123**:751–762. doi: 10.1111/j.1469-8137.1993.tb03786.x.

Hedges LV, Gurevitch J, Curtis PS. 1999. The meta-analysis of response ratios in experimental ecology. *Ecology* **80**:1150–1156. doi: 10.1890/0012-9658(1999)080[1150:TMAORR]2.0.CO;2.

Hersoug L-G, Sjödin A, Astrup A. 2012. A proposed potential role for increasing atmospheric CO_2 as a promoter of weight gain and obesity. *Nutrition & Diabetes* **2**:e31. doi: 10.1038/nutd.2012.2.

Hill JO, Wyatt HR, Reed GW, Peters JC. 2003. Obesity and the environment: where do we go from here? *Science* **299**:853–855. doi: 10.1126/science.1079857.

Högy P, Brunnbauer M, Koehler P, Schwadorf K, Breuer J, Franzaring J, Zhunusbayeva D, Fangmeier A. 2013. Grain quality characteristics of spring wheat (*Triticum aestivum*) as affected by free-air CO_2 enrichment. *Environmental and Experimental Botany* **88**:11–18. doi: 10.1016/j.envexpbot.2011.12.007.

Högy P, Fangmeier A. 2009. Atmospheric CO2 enrichment affects potatoes: 2. Tuber quality traits. *European Journal of Agronomy* **30**:85–94. doi: 10.1016/j.eja.2008.07.006.

Högy P, Franzaring J, Schwadorf K, Breuer J, Schütze W, Fangmeier A. 2010. Effects of free-air CO2 enrichment on energy traits and seed quality of oilseed rape. *Agriculture, Ecosystems & Environment* **139**:239–244. doi: 10.1016/j.agee.2010.08.009.

Högy P, Wieser H, Köhler P. 2008. Does elevated atmospheric CO2 allow for sufficient wheat grain quality in the future? *Journal of Applied Botany and Food Quality* **82**:114–121. doi: 10.5073/jabfq.2089.82.2.114-121.

Högy P, Wieser H, Köhler P, Schwadorf K, Breuer J, Franzaring J, Muntifering R, Fangmeier A. 2009. Effects of elevated CO2 on grain yield and quality of wheat: results from a 3-year free-air CO2 enrichment experiment. *Plant Biology* **11**(Suppl 1):60–69. doi: 10.1111/j.1438-8677.2009.00230.x.

Housman DC, Killingbeck KT, Dave Evans R, Charlet TN, Smith SD. 2012. Foliar nutrient resorption in two Mojave Desert shrubs exposed to Free-Air CO2 Enrichment (FACE). *Journal of Arid Environments* **78**:26–32. doi: 10.1016/j.jaridenv.2011.11.007.

Huluka G, Hileman D, Biswas P, Lewin K, Nagy J, Hendrey G. 1994. Effects of elevated CO2 and water stress on mineral concentration of cotton. *Agricultural and Forest Meteorology* **70**:141–152. doi: 10.1016/0168-1923(94)90053-1.

Hungate BA, Stiling PD, Dijkstra P, Johnson DW, Ketterer ME, Hymus GJ, Hinkle CR, Drake BG. 2004. CO2 elicits long-term decline in nitrogen fixation. *Science* **304**:1291. doi: 10.1126/science.1095549.

Ioannidis JPA. 2005. Why most published research findings are false. *PLOS Medicine* **2**:e124. doi: 10.1371/journal.pmed.0020124.

IPCC. 2007. Climate change 2007: synthesis report. *An Assessment of the Intergovernmental Panel on Climate Change*. URL https://www.ipcc.ch/pdf/assessment-report/ar4/syr/ar4_syr.pdf

IPCC. 2013. Climate change 2013. The physical science Basis. Working group I Contribution to the IPCC Fifth assessment report. *Summary for Policymakers*. URL http://www.climatechange2013.org/images/report/WG1AR5_SPM_FINAL.pdf

Jablonski LM, Wang X, Curtis PS. 2002. Plant reproduction under elevated CO2 conditions: a meta-analysis of reports on 79 crop and wild species. *New Phytologist* **156**:9–26. doi: 10.1046/j.1469-8137.2002.00494.x.

Jain V, Pal M, Raj A, Khetarpal S. 2007. Photosynthesis and nutrient composition of spinach and fenugreek grown under elevated carbon dioxide concentration. *Biologia Plantarum* **51**:559–562. doi: 10.1007/s10535-007-0122-9.

Jia H, Guo H, Yin Y, Wang Q, Sun Q, Wang X, Zhu J. 2007. Responses of rice growth to copper stress under free-air CO2 enrichment (FACE). *Chinese Science Bulletin* **52**:2636–2641. doi: 10.1007/s11434-007-0362-2.

Jin CW, Du ST, Chen WW, Li GX, Zhang YS, Zheng SJ. 2009. Elevated carbon dioxide improves plant iron nutrition through enhancing the iron-deficiency-induced responses under iron-limited conditions in tomato. *Plant Physiology* **150**:272–280. doi: 10.1104/pp.109.136721.

Johnson D, Ball J, Walker R. 1997. Effects of CO2 and nitrogen fertilization on vegetation and soil nutrient content in juvenile ponderosa pine. *Plant and Soil* **190**:29–40. doi: 10.1023/A:1004213826833.

Johnson DW, Cheng W, Joslin JD, Norby RJ, Edwards NT, Todd DE. 2004. Effects of elevated CO2 on nutrient cycling in a sweetgum plantation. *Biogeochemistry* **69**:379–403. doi: 10.1023/B:BIOG.0000031054.19158.7c.

Johnson DW, Hungate BA, Dijkstra P, Hymus G, Hinkle CR, Stiling P, Drake BG. 2003. The effects of elevated CO2 on nutrient distribution in a fire-adapted scrub oak forest. *Ecological Applications* **13**:1388–1399. doi: 10.1890/02-5139.

Jonard M, André F, Dambrine E, Ponette Q, Ulrich E. 2009. Temporal trends in the foliar nutritional status of the French, Walloon and Luxembourg broad-leaved plots of forest monitoring. *Annals of Forest Science* **66**:412–412. doi: 10.1051/forest/2009014.

Kanowski J. 2001. Effects of elevated CO2 on the foliar chemistry of seedlings of two rainforest trees from north-east Australia: implications for folivorous marsupials. *Austral Ecology* **26**:165–172. doi: 10.1046/j.1442-9993.2001.01103.x.

Katny MAC, Hoffmann-Thoma G, Schrier AA, Fangmeier A, Jäger H-J, van Bel AJE. 2005. Increase of photosynthesis and starch in potato under elevated CO2 is dependent on leaf age. *Journal of Plant Physiology* **162**:429–438. doi: 10.1016/j.jplph.2004.07.005.

Keats S, Wiggins S. 2014. Future diets. *Implications for agriculture and food prices*, London: Overseas Development Institute. Report.

Keenan TF, Hollinger DY, Bohrer G, Dragoni D, Munger JW, Schmid HP, Richardson AD. 2013. Increase in forest water-use efficiency as atmospheric carbon dioxide concentrations rise. *Nature* **499**:324–327. doi: 10.1038/nature12291.

Kennedy G, Nantel G, Shetty P. 2003. The scourge of "hidden hunger": global dimensions of micronutrient deficiencies. *Food Nutrition and Agriculture* **32**:8–16.

Keutgen N, Chen K. 2001. Responses of citrus leaf photosynthesis, chlorophyll fluorescence, macronutrient and carbohydrate contents to elevated CO2. *Journal of Plant Physiology* **158**:1307–1316. doi: 10.1078/0176-1617-00564.

Keutgen N, Chen K, Lenz F. 1997. Responses of strawberry leaf photosynthesis, chlorophyll fluorescence and macronutrient contents to elevated CO2. *Journal of Plant Physiology* **150**:395–400. doi: 10.1016/S0176-1617(97)80088-0.

Khan I, Azam A, Mahmood A. 2013. The impact of enhanced atmospheric carbon dioxide on yield, proximate composition, elemental concentration, fatty acid and vitamin C contents of tomato (*Lycopersicon esculentum*). *Environmental Monitoring and Assessment* **185**:205–214. doi: 10.1007/s10661-012-2544-x.

Khokhar S, Garduño-Diaz SD, Marletta L, Shahar DR, Ireland JD, Jansen-van der Vliet M, de Henauw S. 2012. Mineral composition of commonly consumed ethnic foods in Europe. *Food & Nutrition Research* **56**:1–8. doi: 10.3402/fnr.v56i0.17665.

Klimentidis YC, Beasley TM, Lin H-Y, Murati G, Glass GE, Guyton M, Newton W, Jorgensen M, Heymsfield SB, Kemnitz J, Fairbanks L, Allison DB. 2011. Canaries in the coal mine: a cross-species analysis of the plurality of obesity epidemics. *Proceedings Biological Sciences/the Royal Society* **278**:1626–1632. doi: 10.1098/rspb.2010.1890.

Koh KA, Hoy JS, O'Connell JJ, Montgomery P. 2012. The Hunger-obesity paradox: obesity in the homeless. *Journal of Urban Health* **89**:952–964. doi: 10.1007/s11524-012-9708-4.

Kuehny JS, Peet MM, Nelson PV, Willits DH. 1991. Nutrient dilution by starch in CO2 -enriched Chrysanthemum. *Journal of Experimental Botany* **42**:711–716. doi: 10.1093/jxb/42.6.711.

Lahner B, Gong J, Mahmoudian M, Smith EL, Abid KB, Rogers EE, Guerinot ML, Harper JF, Ward JM, McIntyre L, Schroeder JI, Salt DE. 2003. Genomic scale profiling of nutrient and trace elements in *Arabidopsis thaliana*. *Nature Biotechnology* **21**:1215–1221. doi: 10.1038/nbt865.

Leakey ADB, Ainsworth EA, Bernacchi CJ, Rogers A, Long SP, Ort DR. 2009. Elevated CO2 effects on plant carbon, nitrogen, and water relations: six important lessons from FACE. *Journal of Experimental Botany* **60**:2859–2876. doi: 10.1093/jxb/erp096.

Li J, Zhou J-M, Duan Z-Q, Du C-W, Wang H-Y. 2007. Effect of CO2 enrichment on the growth and nutrient uptake of tomato seedlings. *Pedosphere* **17**:343–351. doi: 10.1016/S1002-0160(07)60041-1.

Li Z, Tang S, Deng X, Wang R, Song Z. 2010. Contrasting effects of elevated CO2 on Cu and Cd uptake by different rice varieties grown on contaminated soils with two levels of metals: implication for phytoextraction and food safety. *Journal of Hazardous Materials* **177**:352–361. doi: 10.1016/j.jhazmat.2009.12.039.

Lieffering M, Kim H-Y, Kobayashi K, Okada M. 2004. The impact of elevated CO2 on the elemental concentrations of field-grown rice grains. *Field Crops Research* **88**:279–286. doi: 10.1016/j.fcr.2004.01.004.

Loladze I. 2002. Rising atmospheric CO2 and human nutrition: toward globally imbalanced plant stoichiometry? *Trends in Ecology & Evolution* **17**:457–461. doi: 10.1016/S0169-5347(02)02587-9.

Luomala E, Laitinen K, Sutinen S, Kellomaki S, Vapaavuori E, Kellomäki S. 2005. Stomatal density, anatomy and nutrient concentrations of Scots pine needles are affected by elevated CO2 and temperature. *Plant, Cell & Environment* **28**:733–749. doi: 10.1111/j.1365-3040.2005.01319.x.

Ma H, Zhu J, Xie Z, Liu G, Zeng Q, Han Y. 2007. Responses of rice and winter wheat to free-air CO2 enrichment (China FACE) at rice/wheat rotation system. *Plant and Soil* **294**:137–146. doi: 10.1007/s11104-007-9241-5.

Manderscheid R, Bender J, Jäger H-J, Weigel HJ. 1995. Effects of season long CO2 enrichment on cereals. II. Nutrient concentrations and grain quality. *Agriculture, Ecosystems & Environment* **54**:175–185. doi: 10.1016/0167-8809(95)00602-O.

Manoj-Kumar. 2011. Will rising CO2 affect Zn and Fe bioavailability in food grains? *Current Science* **101**:467. doi: 10.1080/17429145.2010.513483.

Martin J, Wang ZQ, Zhang XH, Wachtel D, Volaufova J, Matthews DE, Cefalu WT. 2006. Chromium picolinate supplementation attenuates body weight gain and increases insulin sensitivity in subjects with type 2 diabetes. *Diabetes Care* **29**:1826–1832. doi: 10.2337/dc06-0254.

McGrath JM, Lobell DB. 2013. Reduction of transpiration and altered nutrient allocation contribute to nutrient decline of crops grown in elevated CO2 concentrations. *Plant, Cell & Environment* **36**:697–705. doi: 10.1111/pce.12007.

McKeehen JD, Smart DJ, Mackowiak CL, Wheeler RM, Nielsen SS. 1996. Effect of CO2 levels on nutrient content of lettuce and radish. *Advances in Space Research* **18**:85–92. doi: 10.1016/0273-1177(95)00864-B.

Mishra S, Heckathorn SA, Frantz JM. 2011. Elevated CO2 affects plant responses to variation in boron availability. *Plant and Soil* **350**:117–130. doi: 10.1007/s11104-011-0888-6.

Mjwara JM, Botha CEJ, Radloff SE. 1996. Photosynthesis, growth and nutrient changes in non-nodulated *Phaseolus vulgaris* grown under atmospheric and elevated carbon dioxide conditions. *Physiologia Plantarum* **97**:754–763. doi: 10.1111/j.1399-3054.1996.tb00541.x.

Natali SM, Sañudo-Wilhelmy SA, Lerdau MT. 2009. Plant and soil mediation of elevated CO2 impacts on trace metals. *Ecosystems* **12**:715–727. doi: 10.1007/s10021-009-9251-7.

Newbery R, Wolfenden J, Mansfield T, Harrison A. 1995. Nitrogen, phosphorus and potassium uptake and demand in *Agrostis capillaris*: the influence of elevated CO2 and nutrient supply. *New Phytologist* **130**:565–574. doi: 10.1111/j.1469-8137.1995.tb04333.x.

Niinemets U, Tenhunen JD, Canta NR, Chaves MM, Faria T, Pereira JS, Reynolds JF. 1999. Interactive effects of nitrogen and phosphorus on the acclimation potential of foliage photosynthetic properties of cork oak, *Quercus suber*, to elevated atmospheric CO2 concentrations. *Global Change Biology* **5**:455–470. doi: 10.1046/j.1365-2486.1999.00241.x.

Niu Y, Chai R, Dong H, Wang H, Tang C, Zhang Y. 2013. Effect of elevated CO_2 on phosphorus nutrition of phosphate-deficient *Arabidopsis thaliana* (L.) Heynh under different nitrogen forms. *Journal of Experimental Botany* **64**:355–367. doi: 10.1093/jxb/ers341.

Nowak J, Sroka S, Matysiak B. 2002. Effects of light level, CO2 enrichment, and concentration of nutrient solution on growth, leaf nutrient content, and chlorophyll fluorescence of boston fern microcuttings. *Journal of Plant Nutrition* **25**:2161–2171. doi: 10.1081/PLN-120014068.

O'Neill EG, Luxmoore RJ, Norby RJ. 1987. Elevated atmospheric CO2 effects on seedling growth, nutrient uptake, and rhizosphere bacterial populations of *Liriodendron tulipifera* L. *Plant and Soil* **104**:3–11. doi: 10.1007/BF02370618.

Oksanen E, Riikonen J, Kaakinen S, Holopainen T, Vapaavuori E. 2005. Structural characteristics and chemical composition of birch (*Betula pendula*) leaves are modified by increasing CO2 and ozone. *Global Change Biology* **11**:732–748. doi: 10.1111/j.1365-2486.2005.00938.x.

Overdieck D. 1993. Elevated CO2 and the mineral content of herbaceous and woody plants. *Vegetatio* **104–105**:403–411. doi: 10.1007/BF00048169.

Pal M, Karthikeyapandian V, Jain V, Srivastava AC, Anupam Raj, Sengupta UK. 2004. Biomass production and nutritional levels of berseem (*Trifolium alexandrium*) grown under elevated CO2. *Agriculture, Ecosystems & Environment* **101**:31–38. doi: 10.1016/S0167-8809(03)00202-0.

Pal M, Rao L, Srivastava A, Jain V, Sengupta U. 2003. Impact of CO2 enrichment and variable nitrogen supplies on composition and partitioning of essential nutrients of wheat. *Biologia Plantarum* **47**:227–231. doi: 10.1023/B:BIOP.0000022256.60122.fc.

Pang J, Zhu J, Xie Z, Chen G-P, Liu G, Zhang Y. 2005. Effects of elevated pCO2 on nutrient uptake by rice and nutrient contents in rice grain. *Chinese Journal of Rice Science* **19**:350–354.

Payahoo L, Ostadrahimi A, Mobasseri M, Khaje Bishak Y, Farrin N, Asghari Jafarabadi M, Mahluji S. 2013. Effects of zinc supplementation on the anthropometric measurements, lipid profiles and fasting blood glucose in the healthy obese adults. *Advanced Pharmaceutical Bulletin* **3**:161–165. doi: 10.5681/apb.2013.027.

Peet MM, Huber SC, Patterson DT. 1986. Acclimation to high CO2 in monoecious cucumbers. Ii. Carbon exchange rates, enzyme activities, and starch and nutrient concentrations. *Plant Physiology* **80**:63–67. doi: 10.1104/pp.80.1.63.

Peng RD. 2009. Reproducible research and Biostatistics. *Biostatistics* **10**:405–408. doi: 10.1093/biostatistics/kxp014.

Penuelas J, Idso SB, Ribas A, Kimball BA. 1997. Effects of long-term atmospheric CO2 enrichment on the mineral concentration of *Citrus aurantium* leaves. *New Phytologist* **135**:439–444. doi: 10.1046/j.1469-8137.1997.00676.x.

Penuelas J, Matamala R. 1993. Variations in the mineral composition of herbarium plant species collected during the last three centuries. *Journal of Experimental Botany* **44**:1523–1525. doi: 10.1093/jxb/44.9.1523.

Pérez-López U, Miranda-Apodaca J, Mena-Petite A, Muñoz-Rueda A. 2014. Responses of nutrient dynamics in barley seedlings to the interaction of salinity and carbon dioxide enrichment. *Environmental and Experimental Botany* **99**:86–99. doi: 10.1016/j.envexpbot.2013.11.004.

Pfirrmann T, Barnes JD, Steiner K, Schramel P, Busch U, Kuchenhoff H, Payer H-D. 1996. Effects of elevated CO2, O3 and K deficiency on Norway spruce (*Picea abies*): nutrient supply, content and leaching. *New Phytologist* **134**:267–278. doi: 10.1111/j.1469-8137.1996.tb04631.x.

Piikki K, Vorne V, Ojanperä K, Pleijel H. 2007. Impact of elevated O3 and CO2 exposure on potato (*Solanum tuberosum* L. cv. Bintje) tuber macronutrients (N, P, K, Mg, Ca). *Agriculture, Ecosystems & Environment* **118**:55–64. doi: 10.1016/j.agee.2006.04.012.

Pleijel H, Danielsson H. 2009. Yield dilution of grain Zn in wheat grown in open-top chamber experiments with elevated CO2 and O3 exposure. *Journal of Cereal Science* **50**:278–282. doi: 10.1016/j.jcs.2009.06.009.

Polley HW, Fay PA, Jin VL, Combs GF. 2011. CO2 enrichment increases element concentrations in grass mixtures by changing species abundances. *Plant Ecology* **212**:945–957. doi: 10.1007/s11258-010-9874-y.

Poorter H, Van Berkel Y, Baxter R, Den Hertog J, Dijkstra P, Gifford RM, Griffin KL, Roumet C, Roy J, Wong SC. 1997. The effect of elevated CO2 on the chemical composition and construction costs of leaves of 27 C3 species. *Plant, Cell & Environment* **20**:472–482. doi: 10.1046/j.1365-3040.1997.d01-84.x.

Poorter H, Villar R. 1997. The fate of acquired carbon in plants: chemical composition and construction costs. In: Bazzaz FA, Grace J (Eds), *Plant resource allocation*. San Diego: Academic Press. p. 39–72. doi: 10.1016/B978-012083490-7/50003-7.

Porteaus F, Hill J, Ball AS, Pinter PJ, Kimball BA, Wall GW, Adamsen FJ, Hunsaker DJ, LaMorte RL, Leavitt SW, Thompson TL, Matthias AD, Brooks TJ, Morris CF. 2009. Effect of Free Air Carbon dioxide Enrichment (FACE) on the chemical composition and nutritive value of wheat grain and straw. *Animal Feed Science and Technology* **149**:322–332. doi: 10.1016/j.anifeedsci.2008.07.003.

Porter MA, Grodzinski B. 1984. Acclimation to high CO2 in bean: Carbonic anhydrase and ribulose bisphosphate carboxylase. *Plant Physiology* **74**:413–416. doi: 10.1104/pp.74.2.413.

Prior SA, Runion GB, Rogers HH, Torbert HA. 2008. Effects of atmospheric CO2 enrichment on crop nutrient dynamics under no-till conditions. *Journal of Plant Nutrition* **31**:758–773. doi: 10.1080/01904160801928364.

R Core Team. 2014. R: a language and environment for statistical computing. *R Foundation for Statistical Computing*. Vienna, Austria. URL http://www.R-project.org/

Rayman MP. 2007. The use of high-selenium yeast to raise selenium status: how does it measure up? *British Journal of Nutrition* **92**:557. doi: 10.1079/BJN20041251.

Razzaque MA, Haque MM, Khaliq QA, Solaiman ARM. 2009. The effect of different nitrogen levels and enrichment CO2 on the nutrient contents of rice cultivars. *Bangladesh Journal of Scientific and Industrial Research* **44**:241–246.

Robinson EA, Ryan GD, Newman JA. 2012. A meta-analytical review of the effects of elevated CO2 on plant-arthropod interactions. *The New Phytologist* **194**:321–336. doi: 10.1111/j.1469-8137.2012.04074.x.

Rodenkirchen H, Göttlein A, Kozovits AR, Matyssek R, Grams TEE. 2009. Nutrient contents and efficiencies of beech and spruce saplings as influenced by competition and O3/CO2 regime. *European Journal of Forest Research* **128**:117–128. doi: 10.1007/s10342-008-0221-y.

Rodriguez JH, Klumpp A, Fangmeier A, Pignata ML. 2011. Effects of elevated CO2 concentrations and fly ash amended soils on trace element accumulation and translocation among roots, stems and seeds of *Glycine max* (L.) Merr. *Journal of Hazardous Materials* **187**:58–66. doi: 10.1016/j.jhazmat.2010.11.068.

Rohde R, Muller RA, Jacobsen R, Muller E, Perlmutter S, Rosenfeld A, Wurtele J, Groom D, Wickham C. 2013. A new estimate of the Average Earth Surface Land Temperature Spanning 1753 to 2011. *Geoinformatics & Geostatistics* **01**:1771–1789. doi: 10.4172/2327-4581.1000101.

Rosenberg MS, Adams DC, Gurevitch J. 2000. *MetaWin: statistical software for meta-analysis*. Sunderland, Massachusetts: Sinauer Associates. URL http://www.metawinsoft.com/

Roumet C, Laurent G, Roy J. 1999. Leaf structure and chemical composition as affected by elevated CO2: genotypic responses of two perennial grasses. *New Phytologist* **143**:73–81. doi: 10.1046/j.1469-8137.1999.00437.x.

Salt DE, Baxter I, Lahner B. 2008. Ionomics and the study of the plant ionome. *Annual Review of Plant Biology* **59**:709–733. doi: 10.1146/annurev.arplant.59.032607.092942.

Schaffer B, Whiley A. 1997. Leaf gas exchange, dry matter partitioning, and mineral element concentrations in mango as influenced by elevated atmospheric carbon dioxide and root restriction. *Journal of the American Society for Horticultural Science* **122**:849–855.

Scheier LM. 2005. What is the hunger-obesity paradox? *Journal of the Academy of Nutrition and Dietetics* **105**:883–884, 886. doi: 10.1016/j.jada.2005.04.013.

Schenk U, Jager H-J, Weigel H-J. 1997. The response of perennial ryegrass/white clover mini-swards to elevated atmospheric CO2 concentrations: effects on yield and fodder quality. *Grass and Forage Science* **52**:232–241. doi: 10.1046/j.1365-2494.1997.00069.x.

Seneweera SP, Conroy JP. 1997. Growth, grain yield and quality of rice (*Oryza sativa* L.) in response to elevated CO2 and phosphorus nutrition. *Soil Science and Plant Nutrition* **43**:1131–1136.

Shinano T, Yamamoto T, Tawaraya K, Tadokoro M, Koike T, Osaki M. 2007. Effects of elevated atmospheric CO2 concentration on the nutrient uptake characteristics of Japanese larch (*Larix kaempferi*). *Tree Physiology* **27**:97–104. doi: 10.1093/treephys/27.1.97.

Shipley B, Lechowicz M, Dumont S, Hendershot WH. 1992. Interacting effects of nutrients, pH - al and elevated CO2 on the growth of red spruce (*Picea rubens* Sarg.) seedlings. *Water, Air, & Soil Pollution* **64**:585–600. doi: 10.1007/BF00483368.

Siegenthaler U, Stocker TF, Monnin E, Lüthi D, Schwander J, Stauffer B, Raynaud D, Barnola JM, Fischer H, Masson-Delmotte V, Jouzel J. 2005. Stable carbon cycle-climate relationship during the Late Pleistocene. *Science* **310**:1313–1317. doi: 10.1126/science.1120130.

Simpson SJ, Raubenheimer D. 2005. Obesity: the protein leverage hypothesis. *Obesity Reviews* **6**:133–142. doi: 10.1111/j.1467-789X.2005.00178.x.

Singh R, Beegom R, Rastogi S, Gaoli Z, Shoumin Z. 1998. Association of low plasma concentrations of antioxidant vitamins, magnesium and zinc with high body fat per cent measured by bioelectrical impedance analysis in Indian men. *Magnesium Research* **11**:3–10.

Singh S, Bhatia A, Tomer R, Kumar V, Singh B, Singh SD. 2013. Synergistic action of tropospheric ozone and carbon dioxide on yield and nutritional quality of Indian mustard (*Brassica juncea* (L.) Czern.). *Environmental Monitoring and Assessment* **185**:6517–6529. doi: 10.1007/s10661-012-3043-9.

Stefan K, Fürst A, Hacker R, Bartels U. 1997. Needle/leaf interlaboratory test 1995/1996. In: United Nations Economic Commision for Europe, *Forest Foliar Condition in Europe Results: Results of large-scale foliar chemistry surveys 1995*. European Commission, Brussels.

Stein AJ. 2009. Global impacts of human mineral malnutrition. *Plant and Soil* **335**:133–154. doi: 10.1007/s11104-009-0228-2.

Sterner RW, Elser JJ. 2002. *Ecological stoichiometry: the biology of elements from molecules to the biosphere*. Princeton, NJ, USA: Princeton University Press. p. 584.

Stiling PD, Cornelissen T. 2007. How does elevated carbon dioxide (CO2) affect plant–herbivore interactions? *Global Change Biology* **13**:1823–1842. doi: 10.1111/j.1365-2486.2007.01392.x.

Still CJ, Berry JA, Collatz GJ, DeFries RS. 2003. Global distribution of C3 and C4 vegetation: carbon cycle implications. *Global Biogeochemical Cycles* **17**:6–1. doi: 10.1029/2001GB001807.

Taub DR, Miller B, Allen H. 2008. Effects of elevated CO2 on the protein concentration of food crops: a meta-analysis. *Global Change Biology* **14**:565–575. doi: 10.1111/j.1365-2486.2007.01511.x.

Taubes G. 2013. The science of obesity: what do we really know about what makes us fat? *British Medical Journal* **346**:f1050. doi: 10.1136/bmj.f1050.

Temperton VM, Grayston SJ, Jackson G, Barton CVM, Millard P, Jarvis PG. 2003. Effects of elevated carbon dioxide concentration on growth and nitrogen fixation in *Alnus glutinosa* in a long-term field experiment. *Tree Physiology* **23**:1051–1059. doi: 10.1093/treephys/23.15.1051.

Teng N, Wang J, Chen T, Wu X, Wang Y, Lin J. 2006. Elevated CO2 induces physiological, biochemical and structural changes in leaves of *Arabidopsis thaliana*. *The New Phytologist* **172**:92–103. doi: 10.1111/j.1469-8137.2006.01818.x.

Tian S, Jia Y, Ding Y, Wang R, Feng R, Song Z, Guo J, Zhou L. 2014. Elevated atmospheric CO2 enhances copper uptake in crops and pasture species grown in copper-contaminated soils in a micro-plot study. *CLEAN–Soil, Air, Water* **42**:347–354. doi: 10.1002/clen.201200401.

Tremblay N, Yelle S, Gosselin A. 1988. Effects of CO2 enrichment, nitrogen and phosphorus fertilization during the nursery period on mineral composition of celery. *Journal of Plant Nutrition* **11**:37–49. doi: 10.1080/01904168809363783.

UNICEF. 2009. Investing in the future: a united call to action on vitamin and mineral deficiencies: global report. micronutrient initiative. Ontario. URL http://www.unitedcalltoaction.org/documents/Investing_in_the_future.pdf

Utriainen J, Janhunen S, Helmisaari H-S, Holopainen T. 2000. Biomass allocation, needle structural characteristics and nutrient composition in Scots pine seedlings exposed to elevated CO2 and O3 concentrations. *Trees* **14**:475–484. doi: 10.1007/s004680000062.

Walker RF, Johnson DW, Geisinger DR, Ball JT. 2000. Growth, nutrition, and water relations of ponderosa pine in a field soil as influenced by long-term exposure to elevated atmospheric CO2. *Forest Ecology and Management* **137**:1–11. doi: 10.1016/S0378-1127(99)00308-4.

Weigt RB, Raidl S, Verma R, Rodenkirchen H, Göttlein A, Agerer R. 2011. Effects of twice-ambient carbon dioxide and nitrogen amendment on biomass, nutrient contents and carbon costs of Norway spruce seedlings as influenced by mycorrhization with *Piloderma croceum* and *Tomentellopsis submollis*. *Mycorrhiza* **21**:375–391. doi: 10.1007/s00572-010-0343-1.

Welch RM, Graham RD. 1999. A new paradigm for world agriculture: meeting human needs. *Field Crops Research* **60**:1–10. doi: 10.1016/S0378-4290(98)00129-4.

Welch RM, Graham RD. 2005. Agriculture: the real nexus for enhancing bioavailable micronutrients in food crops. *Journal of Trace Elements in Medicine and Biology* **18**:299–307. doi: 10.1016/j.jtemb.2005.03.001.

Wells JCK. 2013. Obesity as malnutrition: the dimensions beyond energy balance. *European Journal of Clinical Nutrition* **67**:507–512. doi: 10.1038/ejcn.2013.31.

White PJ, Broadley MR. 2009. Biofortification of crops with seven mineral elements often lacking in human diets–iron, zinc, copper, calcium, magnesium, selenium and iodine. *The New Phytologist* **182**:49–84. doi: 10.1111/j.1469-8137.2008.02738.x.

WHO. 2002. The world health report 2002-reducing risks, promoting healthy life. Geneva. URL http://www.who.int/whr/2002/en/

WHO. 2014. Draft guideline: sugars intake for adults and children. p. 1–48. URL http://www.who.int/nutrition/sugars_public_consultation/en/

Wilsey BJ, McNaughton SJ, Coleman JS. 1994. Will increases in atmospheric CO2 affect regrowth following grazing in C4 grasses from tropical grasslands? A test with *Sporobolus kentrophyllus*. *Oecologia* **99**:141–144. doi: 10.1007/BF00317094.

Woodin S, Graham B, Killick A, Skiba U, Cresser M. 1992. Nutrient limitation of the long term response of heather [*Calluna vulgaris* (L.) Hull] to CO2 enrichment. *New Phytologist* **122**:635–642. doi: 10.1111/j.1469-8137.1992.tb00091.x.

Wroblewitz S, Hüther L, Manderscheid R, Weigel H-J, Wätzig H, Dänicke S. 2013. The effect of free air carbon dioxide enrichment and nitrogen fertilisation on the chemical composition and nutritional value of wheat and barley grain. *Archives of Animal Nutrition* **67**:263–278. doi: 10.1080/1745039X.2013.821781.

Wu D-X, Wang G-X, Bai Y-F, Liao J-X. 2004. Effects of elevated CO2 concentration on growth, water use, yield and grain quality of wheat under two soil water levels. *Agriculture, Ecosystems & Environment* **104**:493–507. doi: 10.1016/j.agee.2004.01.018.

Yamakawa Y, Saigusa M, Okada M, Kobayashi K. 2004. Nutrient uptake by rice and soil solution composition under atmospheric CO2 enrichment. *Plant and Soil* **259**:367–372. doi: 10.1023/B:PLSO.0000020988.18365.b5.

Yan X, Yu D, Li Y-K. 2006. The effects of elevated CO2 on clonal growth and nutrient content of submerge plant *Vallisneria spinulosa*. *Chemosphere* **62**:595–601. doi: 10.1016/j.chemosphere.2005.06.018.

Yang L, Wang Y, Dong G, Gu H, Huang J, Zhu J, Yang H, Liu G, Han Y. 2007. The impact of free-air CO2 enrichment (FACE) and nitrogen supply on grain quality of rice. *Field Crops Research* **102**:128–140. doi: 10.1016/j.fcr.2007.03.006.

Yerlikaya FH, Toker A, Arıbaş A. 2013. Serum trace elements in obese women with or without diabetes. *The Indian Journal of Medical Research* **137**:339–345.

Zheng J, Wang H, Li Z, Tang S, Chen Z. 2008. Using elevated carbon dioxide to enhance copper accumulation in *Pteridium revolutum*, a copper-tolerant plant, under experimental conditions. *International Journal of Phytoremediation* **10**:161–172. doi: 10.1080/15226510801913934.

Ziska L, Namuco O, Moya T, Quilang J. 1997. Growth and yield response of field-grown tropical rice to increasing carbon dioxide and air temperature. *Agronomy Journal* **89**:45–53. doi: 10.2134/agronj1997.00021962008900010007x.