**Supplementary Information**

**Supplementary file 1 – pair-feeding protocol**

The food allocation for the pair-fed group was based on the average consumption of the CIT group from the previous monitoring period + a predicted increase in food consumption (as rats were in a growth phase) ± a correction to ensure that the cumulative food intake remained equal between the CIT and pair-fed groups.

**Supplementary file 2 – Bone mechanical testing – 3 point bend**

Each tibia was rehydrated overnight in phosphate buffered saline (PBS) at room temperature prior to testing. To determine the mechanical properties of cortical bone each tibia was loaded to failure at 0.5 mm/s using a Bose Biodynamic 5500 Test Instrument (Bose, DE, USA). The span between the lower supports was 10 mm. Prior to testing, the tibiae were kept moist in gauze swabs soaked in PBS. Bones were positioned such that the load was applied 8.75 mm from the top of distal condyle in the anterior-posterior (AP) direction with distal condyle facing downwards. WinTest software (WinTest 7) was used to collect the load-displacement data across 10 s with a sampling rate of 250 Hz. Structural properties including Ultimate force (FU; N), yield force (FY; N), stiffness (S; N/mm), and energy (work) to failure (U; mJ) endured by the tibia were calculated from the load and displacement data. The yield point was determined from the load displacement curve at the point at which the curve deviated from linear. Widths of the cortical mid-shaft in the medio-lateral (ML) and antero-posterior (AP) directions, moment of inertia (Imin), and the average cortical thickness were determined byμCT in the cortical region. Tibial material properties, i.e., stress-strain curves were calculated from the structural properties (i.e., load-displacement curve) in combination with morphological data from μCT. The obtained stress-strain curves reflect the stiffness, strength and failure properties of the bone material itself without the influence of geometry.

**Supplementary file 3 – Statistical tests**

**Aim 1 – what is the metabolic and energy balance phenotype arising from inhalant abuse and does it persist into abstinence?**

All food intake, water intake and growth measures were analysed as a RM ANOVA (time and group) with Tukey’s post-hoc testing. Bomb calorimetry results were analysed using a one-way ANOVA with Tukey’s post-hoc at the end of both exposure and abstinence. 3-bottle choice was analysed using a two-way ANOVA (liquid and group) with Tukey’s post-hoc testing. Metabolic cage repeated measures data were analysed as a RM ANOVA (time and group) with Tukey’s post-hoc testing. Food and water totals consumed within the metabolic cages were analysed with independent samples t-tests. Blood glucose, insulin, and leptin levels were analysed as a two-way ANOVA (fed-state and group) with Tukey’s post-hoc. Liver glycogen levels were analysed as a one-way ANOVA (by group) with Tukey’s post-hoc. All skeletal variables were measured as a one-way ANOVA (by group) with Tukey’s post-hoc.

**Aim 2 – is adrenal insufficiency present following adolescent inhalant abuse?**

Post-mortem organ weights were analysed with ANCOVA, with body weight as the co-variate. Adrenal histology results were analysed with independent sample t-tests. Basal corticosterone and ACTH results were analysed with independent sample t-tests. Variables within the ITT and stress response test were all measured as a two-way ANOVA (time and group).

**Supplementary file 4 – additional food and water intake results**

There were no significant group differences in food intake when corrected for body weight, during either exposure or abstinence (Supplementary Figure 1A). Daily water intake was increased in the CIT group compared to both Air-controls and Pair-fed during the exposure period (F=5.465 p=0.01, Supplementary Figure 1B) with no group differences at the end of the abstinence period. When corrected for body weight, water intake was again significantly higher in the CIT group in the exposure period (F=16.946 p<0.000, Supplementary Figure 1C) which remained significant into the abstinence period (F=6.934 p=0.003, Supplementary Figure 1C). There were no significant group differences in the conversion of food to body weight during the exposure period, though the Pair-fed had a significantly higher conversion of food to body weight during the abstinence period (F=4.790 p=0.016, Supplementary Figure 1D).

[Supplementary Figure 1 here]

Supplementary Figure 1. A) There were no significant group differences in food intake when corrected for body weight. B) Daily water intake was higher in the CIT group compared to both Air-controls and Pair-fed during the exposure, but not abstinence period. C) Daily water intake when corrected for body weight was higher in the CIT group compared to Air-controls and Pair-fed through exposure and abstinence D) There were no group differences in the conversion of food to body weight during the exposure period, but the Pair-fed group was significantly higher than Air-controls and CIT during the abstinence period. \*p<0.05, \*\*\*p<0.001 (CIT significantly different from both Air-controls and Pair-fed). ##p<0.01 (Pair-fed significantly different from Air-controls and CIT). Throughout exposure and abstinence periods (Air-controls n=10, Pair-fed n=10, CIT n=12).

**Supplementary file 5 – additional metabolic cage results**

There were no significant differences in metabolic rate when body weight was not corrected for, in either baseline (Supplementary Figure 2A) or in a fast/re-feeding paradigm (Supplementary Figure 2B). There was also no significant difference in metabolic rate when body weight was corrected for, in a fast/re-feeding paradigm (Supplementary Figure 2C). Similarly, there were no significant differences in energy expenditure when body weight was not corrected for, in either baseline (Supplementary Figure 2D) or in a fast/re-feeding paradigm (Supplementary Figure 2E), or when body weight was corrected for, in a fast/re-feeding paradigm (Supplementary Figure 2F). There were no significant differences in RER under baseline conditions (Supplementary Figure 2G) or water intake under baseline conditions (Supplementary Figure 2H).

[Supplementary Figure 2 here]

Supplementary Figure 2. A) No significant group differences were evident in baseline metabolic rate when body weight is not corrected for. B) No significant group differences were evident in metabolic rate when body weight is not corrected for, in a fast/re-feeding paradigm. C) No significant group differences were evident in metabolic rate when body weight is corrected for, in a fast/re-feeding paradigm. D) No significant group differences were evident in baseline energy expenditure when body weight is not corrected for. E) No significant group differences were evident in energy expenditure when body weight is not corrected for, in a fast/re-feeding paradigm. F) No significant group differences were evident in energy expenditure when body weight is corrected for, in a fast/re-feeding paradigm. G) No significant group differences in baseline respiratory exchange ratio. H) No significant group differences were evident in baseline water intake. Experiment undertaken at end of exposure period (Air-controls n=8, CIT n=8).

**Supplementary file 6 – additional skeletal data**

No significant differences at the end of exposure or abstinence periods were observed by microCT for tibiae length (Supplementary Figure 3A), marrow area (Supplementary Figure 3B), cortical area (Supplementary Figure 3C), endocortical perimeter (Supplementary Figure 3D), periosteal perimeter (Supplementary Figure 3E), or mean polar moment of inertia (Supplementary Figure 3F).

As there had been an observed reduction in cortical thickness in the CIT group only at the end of the abstinence period, the mechanical properties of the bone were tested at that time point. There were no significant differences in material properties of the tibiae at the end of abstinence for variables of Young’s Modulus (Supplementary Figure 4A), Yield Stress (Supplementary Figure 4B), Ultimate Stress (Supplementary Figure 4C) or Failure Stress (Supplementary Figure 4D).

[Supplementary Figure 3 here]

Supplementary Figure 3. No significant group differences were observed at the end of exposure or abstinence for A) tibiae length. B) marrow area. C) cortical area. D) endocortical perimeter. E) periosteal perimeter. F) mean polar moment or inertia. Tibiae were analysed by µCT at the end of the exposure (Air-controls n=10, Pair-fed n=10, CIT n=11) and abstinence periods (Air-controls n=10, Pair-fed n=10, CIT n=12).

[Supplementary Figure 4 here]

Supplementary Figure 4. No significant group differences were observed at the end of abstinence for A) Young’s Modulus. B) Yield Stress. C) Ultimate Stress. D) Failure Stress. Tibiae were mechanically tested at the end of the abstinence period (Air-controls n=10, Pair-fed n=10, CIT n=12).

**Supplementary file 7 – additional adrenal histology data**

In the medulla, the CIT group had a significantly decreased zone width at the end of exposure (t=5.69 p<0.0001, Supplementary Figure 5A), with no significant differences at the end of abstinence, however, the CIT group had a significantly increased cell size in the medulla at the end of exposure (t=3.361 p=0.004, Supplementary Figure 5B), with no differences at the end of abstinence. In the zona glomerulosa there were no group differences in zone width at either time point (Supplementary Figure 5C), however, the CIT group had significantly smaller cell size at the end of exposure (t=2.296 p=0.0339, Supplementary Figure 5D) and abstinence (t=2.618 p=0.0165, Supplementary Figure 5D). In the zona reticularis there were no group differences in zone width at either time point (Supplementary Figure 5E), however, the CIT group had significantly smaller cell size at the end of exposure (t=2.221 p=0.0394, Supplementary Figure 5F) and abstinence (t=2.264 p=0.0349, Supplementary Figure 5F).

[Supplementary Figure 5 here]

Supplementary Figure 5. A) CIT group had a reduced medulla zone width at the end of exposure, but no difference at the end of abstinence. B) CIT group had increased medulla cell size at the end of exposure, but no difference at the end of abstinence. C). There were no group differences in zona glomerulosa width at either time point. D). CIT group had decreased zona glomerulosa cell size at both time points. E). There were no group differences in zona reticularis width at either time point. F) CIT group had decreased zona reticularis cell size at both time points. \* p<0.05, \*\*p<0.01, \*\*\*\*p<0.0001. Adrenal glands collected at the end of the exposure (Air-controls n=10, CIT n=11) and abstinence periods (Air-controls n=10, CIT n=12).