Effects of weight changes in the autonomic nervous system: a systematic review protocol

Reviewers
Costa, JPO¹
Silva, DMGSP¹
¹ Faculty of Medicine, University of Porto

Background

The prevalence of overweight and obese individuals is increasing at an alarming rate throughout the world, in both developed and developing countries. In 2005, it was estimated that 937 million people throughout the world were overweight, and 396 million people were obese. In 2030, the respective number of overweight and obese adults was projected to be 1,35 billion and 573 million individuals.[1] Epidemiologic studies indicate that overweight and obesity are important risk factors for diabetes, cardiovascular disease, cancer and premature death.[2] The rising prevalence and the associated comorbidities will be a major expense in healthcare budgets in developed and developing countries, straining production rates and decreasing workforce vitality, capabilities and quality of life. Despite recent breakthroughs, there is still no pharmacological agent or surgical procedure widely accepted as a gold-standard therapy with intention to cure. So far, the best methods for prevention and management of excess weight and obesity are nutritionally balanced diets and exercise regimens.

The autonomic nervous system (ANS) is the visceral control system of the body, regulating blood vessel tone, heart rate, gastrointestinal function, energy metabolism and hormonal response. A 10% increase in body weight is associated with a decline in parasympathetic tone, accompanied by a rise in mean heart rate, and conversely, heart rate declines during weight reduction.[3] Reductions in vagal activity with increment in weight may be one mechanism for the arrhythmias and other cardiac abnormalities that accompany obesity.[3] Furthermore, the ANS plays an important role in metabolism, and obesity is associated with a relative or absolute reduction in the activity of the thermogenic component of the sympathetic nervous system.[3] Numerous studies have pointed out changes in ANS activity in overweight and obese test subjects, in both humans and animal test models. However, it is still a matter of controversy the physiological effect of dietary and physical activity habits. The inconsistency is thought to arise largely from the difficulty in controlling the arrangement of variables (including genetic differences, physical activity levels, the degree of obesity, dietary and behavioral habits, and emotional stress) and in adequately assessing the SNS activity in human subjects of all age groups.[4]
Given the complexity of the ANS, there is no single test that precisely reflects function of a specific branch of this system.[5] Therefore, it is not uncommon to order numerous tests based on diverse reflexes. Traditionally, research in ANS activity was done by testing the autonomic reflexes (Valsalva manoeuvre, deep breathing, isometric handgrip test, orthostatic test, cold pressure test, among others).[5] More recently, new techniques, such as evaluation of heart rate variability, measurement of neurotransmitter levels and microneurography, have been introduced as research tools.[5, 6]

The aim of this systematic review is to understand the modulation of the activity of sympathetic and parasympathetic nervous systems induced by weight gain and loss resulting from dietary and physical exercise regimens in human subjects. This review also aims to access the baseline activity of ANS in human subjects above and below the normal IMC range.

**Review questions/objectives**

**Population** – Patients who underwent weight change regimen AND Patients who are constitutively above normal weight range AND Patients who are constitutively below normal weight range;

**Interventions** – Weight change regimen (Diet AND Physical exercise);

**Outcomes** – Effects on autonomic nervous system;

**Outcomes measures** – Heart rate spectral analysis, norepinephrine spillover rate, muscle sympathetic nerve activity, pupillometry and resting energy expenditure (REE);

**Study designs** – Randomised controlled trials (RCT), cohort studies, case control studies and case series;

The quantitative objectives are:

- Identify the effect of weight changes in the activity of the autonomic nervous system;
- Identify the effects of the physical condition of people who are constitutively above or below the normal weight range in the activity of the autonomic nervous system;

In patients who underwent a weight change regimen, to what extent did the intervention change the overall activity of the autonomic nervous system? In patients who are constitutively below or above the normal weight range, to what extent does their physical condition changes the basal levels of activity of the autonomic nervous system?

### Inclusion criteria

**Types of participants**

This systematic review will consider all studies that involved human subjects of any age,
gender or ethnicity that were subjected to a weight change regimen that resulted in weight gain or loss. This review will also include all studies that evaluated the basal activity of the autonomic nervous system of human subjects of any age, gender or ethnicity who were above or below the normal BMI ($\geq 25\text{kg/m}^2$ and $\leq 20\text{kg/m}^2$, respectively).

**Types of intervention**

Interventions of interest include weight reduction regimens based upon very low or low calorie intake, other dietary plans and all exercise-based regimens. All types of procedures of bariatric surgery won’t be considered in this study due to their unknown effect in autonomic nervous system activity through altered nutrient absorption and other types of nutritional deficiencies.[7-9]

**Types of outcome measure**

The primary outcome measures are heart rate spectral analysis, norepinephrine spillover rate, muscle sympathetic nerve activity, pupillometry and resting energy expenditure (REE). These are surrogate measures used to evaluate the activity of both sympathetic and parasympathetic nervous systems.

**Types of studies**

This systematic review will consider randomised controlled trials (RCT), cohort studies, case control studies and case series that evaluated the effect of weight change interventions in the activity of the autonomic nervous system and studies that evaluated the basal activity of the autonomic nervous system in people above or below the normal BMI range.

**Search strategy**

The search strategy aims to find both published and unpublished studies. A three-step search strategy will be undertaken in this systematic review, with the following stages:

- The first stage will comprise a limited search of PubMed (1879 to the present) and CINAHL Plus with Full Text (1937 to the present) databases, with subsequent analysis of the title, abstract and index terms of the results. This will allow the identification of relevant keywords.
- The second stage will comprise an extensive search of the literature across all included databases using all identified keywords and index terms.
- The third stage will comprise a search of the reference lists and bibliographies of the articles collected in the second stage.
The initial search query included the terms “weight change” and “autonomic nervous system”. The search strategy is annexed to this protocol.

The following databases will be searched in this review thought the Pubmed, Ebsco, Web of Science and Scopus search engines:

- MEDLINE (1946 to the present) and other citations sources included in PubMed;
- CINAHL Plus with Full Text;
- SPORTDiscus with Full Text (1800 to the present);
- Web of Science™ Core Collection (1900 to the present);
- Scopus (1823 to the present);

Full copies of the articles identified by the search and considered to meet the inclusion criteria based upon the title, abstract and index terms, will be obtained for data synthesis. Articles identified through reference lists and bibliography searches will be considered for inclusion in the next phase based upon their title. Two reviewers will independently select the articles that meet the inclusion criteria. Discrepancies in reviewer selections will be resolved at a meeting between reviewers prior to the extraction of the selected articles.

**Assessment of methodological quality**

The extracted studies that meet the inclusion criteria will be grouped into experimental studies, cohort studies/case control studies and descriptive/case series. Data relating to the methodological quality will be extracted by two reviewers and processed using the Review Manager 5.3 software risk of bias tools. Any discrepancies that arise from the reviewers’ assessment will be resolved at a meeting between reviewers prior to inclusion in the review.

**Data collection**

Quantitative data will be extracted from papers included in the review using the Review Manager 5.3 software data and analysis structure. The data extracted will include specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives, which will be compiled using the characteristics of included studies tables in the aforementioned software. One reviewer will perform data extraction.

**Data synthesis**

Odds ratio (for categorical outcome data) or standardised mean differences (for continuous outcome data) and their 95% confidence intervals of the qualitative data will be calculated, where possible, from the data generated by each of the included studies. If appropriate with available data, results from comparable groups of studies will be pooled through the random-effects model into statistical meta-analysis using Review Manager 5.3 software from the
Cochrane Collaboration. Heterogeneity between combined studies will be tested using standard chi-square test. Where statistical pooling is not possible the findings will be presented in narrative form. The GRADE approach will be used to access the quality of the body of evidence of the outcome across all included studies.

**Potential conflicts of interest**

No conflicts of interest are present.

**References**


**Search strategy - PubMed**

1. Autonomic nervous system
2. Autonomic nervous systems
3. Autonomic pathways
4. Sympathetic nervous system
5. Parasympathetic nervous system
6. ANS
7. Body weight
8. Body weight change
9. Body weight changes
10. Weight gain
11. Weight gains
12. Weight loss
13. Weight reduction
14. Weight increase
15. Overweight
16. Obesity
17. Thin
18. Thinness
19. Animals [mh]
20. Humans [mh]
22. 19. NOT 21.
23. 1. OR 2. OR 3. OR 4. OR 5. OR 6. OR 7.
25. 23. AND 24. NOT 22.

(((Autonomic nervous system) OR Autonomic nervous systems) OR Autonomic pathways) OR Sympathetic nervous system) OR Parasympathetic nervous system) OR ANS)) AND (((((Body weight) OR Body weight change) OR Body weight changes) OR Weight gain) OR Weight gains) OR Weight loss) OR Weight reduction) OR Weight increase) OR Overweight) OR Obesity) OR Thin) OR Thinness))) NOT ((animals [mh] not (humans [mh] and animals [mh])))

Search strategy – Scopus

1. Autonomic nervous system OR Autonomic nervous systems OR Autonomic pathways OR Sympathetic nervous system OR Parasympathetic nervous system OR ANS
2. Body weight OR Body weight change OR Body weight changes OR Weight gain OR Weight gains OR Weight loss OR Weight reduction OR Weight increase OR Overweight OR Obesity OR Thin OR Thinness
3. Animals
4. Animals AND Humans
5. 1. AND 2. AND NOT 3. AND NOT 4.
Search strategy – Web of Science

1. Autonomic nervous system OR Autonomic nervous systems OR Autonomic pathways OR Sympathetic nervous system OR Parasympathetic nervous system OR ANS
2. Body weight OR Body weight change OR Body weight changes OR Weight gain OR Weight gains OR Weight loss OR Weight reduction OR Weight increase OR Overweight OR Obesity OR Thin OR Thinness
3. Animals
4. Animals AND Humans
5. 3. NOT 4.
6. 1. AND 2. NOT 5.

Search strategy – Ebsco

1. Autonomic nervous system OR Autonomic nervous systems OR Autonomic pathways OR Sympathetic nervous system OR Parasympathetic nervous system OR ANS
2. Body weight OR Body weight change OR Body weight changes OR Weight gain OR Weight gains OR Weight loss OR Weight reduction OR Weight increase OR Overweight OR Obesity OR Thin OR Thinness
3. MH Animals
4. MH Animals AND MH Humans
5. 3. NOT 4.
6. 1. AND 2. NOT 5.

(Autonomic nervous system OR Autonomic nervous systems OR Autonomic pathways
OR Sympathetic nervous system OR Parasympathetic nervous system OR ANS) AND
(Body weight OR Body weight change OR Body weight changes OR Weight gain OR
Weight gains OR Weight loss OR Weight reduction OR Weight increase OR
Overweight OR Obesity OR Thin OR Thinness) NOT (MH animals) NOT (MH humans
AND MH animals)