The modification of heart rate variability in normal, overweight and type 2 diabetic individuals.

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"What is this life if full of care;

We have no time to stand and stare."

From the poem Leisure by W H Davies

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List of Abbreviations

ω3	Omega 3
(D)BP	Diastolic Blood Pressure
(S)BP	Systolic Blood Pressure
ANS	Autonomic Nervous System
BMI	Body Mass Index
CAN	Cardiac Autonomic Neuropathy
CSIRO	Commonwealth Scientific and industrial Research Organisation
CVD	Cardiovascular Disease
DAN	Diabetic Autonomic Neuropathy
DHA	Docosahexaenoic Acid
DPA	Docosapentaenoic Acid
ECG	Electrocardiogram
EPA	Eicosapentaenoic Acid
HDL	High Density Lipoprotein
HF(P)	High Frequency Power
HOMA	Homeostasis Model Assessment Index
HR	Heart Rate
HRV	Heart Rate Variability
LF(P)	Low Frequency Power
HUT	Head Up Tilt
IPAQ	International Physical Activity Questionnaire
LBNP	Lower Body Negative Pressure
LDL	Low Density Lipoprotein

LF/HF	Low Frequency to High Frequency ratio
n-3 PUFA	Omega 3 Polyunsaturated Fatty Acid
NO	Nitric oxide
PNS	Parasympathetic Nervous System
PSD	Power Spectral Density
RMSSD	Square Root of the Mean Squared Differences of Successive Normal to Normal Intervals
R-R	Normal to Normal
RSA	Respiratory Sinus Arrhythmia
SDANN	Standard Deviation of the Average Normal to Normal Interval
SDNN	Standard Deviation of the Normal to Normal Interval
SEM	Standard Error of the Mean
SNS	Sympathetic Nervous System
T2D	Type 2 Diabetes Miletus
TAG	Triglycerides
ULF	Ultra Low Frequency
VLF	Very Low Frequency

Summary

The aim of this thesis was to improve our understanding of the effects that dietary therapies have on improving cardiac autonomic activity in healthy and diabetic people, particularly the effects of omega 3 polyunsaturated fatty acids (PUFA) on healthy people. Research conducted to date suggests that diet has specific effects on cardiac autonomic activity; however, much of this research has ignored the underlying influence of specific therapies and weight loss. In this thesis, heart rate variability (HRV) is used to assess cardiac autonomic activity. Cardiac autonomic activity is chiefly responsible for the beat to beat control of heart rate and has been implicated in sudden cardiac death and prognosis of an adverse cardiovacular event following myocardial infarct.

The first experiment was designed to systematically examine the dose-response changes in cardiac ANS activity and vascular compliance after supplementation with omega 3 polyunsaturated fatty acids. In sixty seven overweight middle aged volunteers, HRV, cardiac sympathetic activity (assessed via low frequency component of HRV), parasympathetic activity (assessed by the high frequency component of HRV), Low Frequency/High Frequency (LF/HF) ratio (representing the balance of sympathetic/parasympathetic nervous activity on heart rate), heart rate (HR), arterial compliance, systolic and diastolic blood pressure were assessed during rest. All variables showed the greatest change in the highest dose group. Arterial compliance and the LF/HF ratio changed in a dose-dependent manner with the omega 3 PUFAs. These results suggest that the observed relationships between fish oil dose and changes in arterial compliance and LF/HF suggest that regular fish

oil supplementation can improve the regulation of HR, HRV and consequently blood pressure by increasing parasympathetic regulation of cardiac autonomic tone in a dose-dependent manner

In the second experiment twenty healthy, young male subjects were subjected to graded lower body negative pressure (LBNP) before and after a 6 week dietary supplement intervention of omega 3 PUFAs. Both periods of LBNP were immediately followed by venepuncture to assess lipid and omega 3 content of the blood cells. After the intervention of omega 3 PUFAs an improvement in cardiac autonomic activity (HRV frequency measures) together with a reduction in HR demonstrated that cardiac autonomic activity was improved during rest. Graded LBNP significantly reduced overall HRV and increased the LF/HF ratio of the frequency domain. After the 6 week intervention of omega 3 PUFAs, the autonomic control of heart rate was improved at the highest level of LBNP. Omega 3 PUFAs were significantly increased in the treatment group. In conclusion, the changes in HR and HRV measures during orthostatic stress demonstrated a cardiovascular response likely to be caused by increasing parasympathetic regulation of cardiac autonomic tone in young active males. These mutual changes may reduce CVD risk from an early age and provide further justification for increased intakes of fish oil.

In the third experiment forty nine type 2 diabetic middle aged subjects undertook a 16 week dietary weight loss intervention. Before and after the trial, HRV measures were recorded for 10 minutes while the patients were supine and at rest for 10 minutes followed by venepuncture for metabolic and lipids markers. HRV frequency

and time domain data indicated that weight loss produced an improvement in cardiac autonomic activity and the mean level of cardiac PNS activity (assessed via the root mean square of the successive differences in R-R intervals, RMSSD) during rest. The observed changes in cardiac ANS activity were attributed to weight loss only, despite similar reductions in several metabolic and cardiovascular blood markers. The results of this study suggest that a calorically restricted diet has favourable effects on cardiac ANS activity and implicate weight loss as a mediator of these effects.

The results of this thesis indicate that dietary intervention in people with and without disease, particularly type 2 diabetes, may specifically influence cardiac autonomic activity, which may improve cardiovascular health outcomes. Moreover, the observed effects of diet on cardiac autonomic activity support the notion that weight loss and omega 3 PUFAs have positive cardiovascular health outcomes. The results of the thesis demonstrate that in order to comprehensively understand the effects of dietary therapeutics on cardiac autonomic activity, it is essential that concomitant changes in HRV are considered.

Declaration

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution to Nicholas Sjoberg and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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List of Publications

Sjoberg NJ, Milte CM, Buckley JD, Howe PR, Coates AM, Saint DA. (2010) Dose-dependent increases in heart rate variability and arterial compliance in overweight and obese adults with DHA-rich fish oil supplementation. Br J Nutr;103:243-8.

Sjoberg N, Brinkworth GD, Wycherley TP, Noakes M, Saint DA. Moderate weight loss improves heart rate variability in overweight and obese adults with type 2 diabetes. J Appl Physiol 2011;110:1060-4.

Sjoberg, NJ; Saint, DA. DHA rich fish oils restricts decreases heart rate variability during orthostatic stress in active young males. [Submitted]

Abstracts Published:

Dose-response effect of DHA rich fish oil on resting heart rate and heart rate variability N Sjoberg, C Milte, A Coates, J Buckley, PRC Howe, DA Saint
Asia Pac J Clin Nutr 2007;16 (Suppl 3): S118

Heart Rate Variability but not Corrected QT Interval has a Dose–Response Relationship with Dietary DHA Rich Fish Oil Supplementation in Overweight Humans Nicholas Sjoberg, Catherine Milte, Alison Coates, Jon Buckley, Peter Howe and David Saint Heart, Lung and Circulation, Volume 17, Supplement 3, 2008, Page S234

Conference Presentations:

Australian Society of Medical Research (ASMR) Conference, Adelaide, Australia, 2007. Presentation of: **Dose-Response Effect on Heart Rate Variability After a 12 Week Intervention of DHA Rich Fish Oil** Authors: N Sjoberg, C Milte, A Coates, J Buckley, PRC Howe, DA Saint

Joint New Zealand Nutritional Society & Nutritional Society of Australia Annual Scientific Meeting, Auckland, New Zealand, 2007. Presentation of: **Dose-response Effect of DHA Rich Fish Oil on Heart Rate Variability** Authors: N Sjoberg, C Milte, A Coates, J Buckley, PRC Howe, DA Saint

18th Scientific Meeting of the European Society of Hypertension and the 22nd Scientific Meeting of the International Society of Hypertension, Berlin, Germany, 2008. Presentation of: **Improvements in resting heart rate, heart rate variability and large artery compliance following omega-3 fatty acid supplementation** Authors: N Sjoberg, C Milte, A Coates, J Buckley, PRC Howe, DA Saint

8th International Congress of the International Society for the Study of Fatty Acids and Lipids (ISSFAL). Kansas City, Missouri, USA, 2008. Presentation of: **Dose-dependent effects of docosahexaenoic acid-rich fish oil on cardiovascular and inflammatory biomarkers** Authors: N Sjoberg, C Milte, A Coates, J Buckley, PRC Howe, DA Saint

Cardiac Society of Australia and New Zealand (CSANZ) and the International Society for Heart Research (ISHR) Conference, Adelaide, Australia, 2008 Presentation of: **Heart rate variability but not corrected QT interval has a dose-response relationship with dietary DHA rich fish oil supplementation in overweight humans** Authors: N Sjoberg, C Milte, A Coates, J Buckley, PRC Howe, DA Saint

North American Association for the Study of Obesity's 27th Annual Scientific Meeting of The Obesity Society, Washington D.C., USA, 2009. Presentation of: **Heart rate variability increases with weight loss in overweight and obese adults with type 2 diabetes.** Authors: Sjoberg, N; Wycherley, TP; Brinkworth, GD; Noakes, M; Saint, DA

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