TOWARDS A BALANCED AND ETHICALLY RESPONSIBLE APPROACH TO UNDERSTANDING DIFFERENCES IN SLEEP TIMING

A thesis presented in partial fulfilment of the requirements for the degree of

Doctor of Philosophy
in
Public Health

at Massey University, Sleep/Wake Research Centre
Wellington Campus
New Zealand

Te Hereripine Sarah-Jane Paine
Tūhoe

2006

This thesis is dedicated to my parents, Te Mihikore Agnes and Cliff Paine.
With love and thanks for all of the opportunities you have given to me.

ABSTRACT

The circadian clock defines physiologically optimal times for sleeping, which vary along a continuum of circadian phenotypes from morning- to evening-type. Although different 'chronotypes' can be discriminated reliably by the Morningness/Eveningness Questionnaire (MEQ), there is little published information on their prevalence. The timing of sleep is also heavily influenced by societal norms. However, the relative contribution of circadian physiology versus psychosocial factors is unknown.

This thesis took a multidimensional approach to investigating preferred sleep timing within the general population of New Zealand (30-49 years). A New Zealand version of the MEQ was mailed to a random stratified sample of 5,000 adults living in the Wellington region (55.7% response rate). Using scoring criteria for middle-aged adults, approximately 25% of the population were morning-types and 25% were evening-types.

The sleeping patterns of 15 morning- and 16 evening-types were monitored using actiwatches and sleep diaries. Morning-types slept significantly earlier, but there were no differences in sleep duration or quality. Both chronotypes showed evidence of using the weekend to catch-up on sleep, although this was more evident among evening-types.

Differences between chronotypes were also investigated using the endogenous melatonin rhythm as a circadian phase marker. The timing of the melatonin rhythm was earlier among morning-types, with the difference being greater for melatonin onset, than offset. However, differences between weekday versus weekend sleep explained more of the variability in sleep timing that did circadian phase.

Understanding the genetic differences in the circadian clock is evolving rapidly. While this is of particular scientific interest, little consideration has been given to the ethical implications of this type of work. In the final study, a Kaupapa Māori framework was used to explore Māori hopes and concerns for genetic research in Aotearoa/New Zealand. Thematic analysis indicated that Māori are not anti-science, however there is an urgent need for ethical guidelines that uphold and respect the values of Māori society.

This thesis argues that sleep is a major public health issue for New Zealand. However, a number of challenges must be met to ensure that new scientific knowledge meets the needs and expectations of the community.

ACKNOWLEDGEMENTS

The work and ideas presented in this thesis are but a small indication of the generosity that was extended to me by the individuals who participated in this research. My deepest gratitude to all of those people who freely gave their time to take part in this programme.

This thesis also represents the years of support and friendship which I have received from a number of people, all of whom deserve acknowledgement in this small way.

I am deeply indebted to my supervisor Professor Philippa Gander, whose unquestioning belief in her staff and students is perhaps only surpassed by her passion for science. Thank-you Philippa for encouraging me to be ambitious, and most of all for letting me carry-out this work the only way I knew how.

I am also extremely grateful for the mentorship I have received from Drs. Papaarangi Reid, Fiona Cram, and Ricci Harris. Their combined knowledge and belief in Kaupapa Māori research has opened my mind and helped me navigate the theoretical journey that was needed for this thesis.

While the Sleep/Wake Research Centre is the embodiment of Philippa's desire for excellence in research, there is no doubt that the quality of the work that is done there is but a symbol of the dedication, motivation, and the character of the people who fill that space. To my friends and colleagues: Kara Mihaere, Riz Firestone, Leigh Signal, Margo van den Berg, Noemie Travier, Sandy Garden, Allison Clarke, Nat Marshall, and the many others who have come and gone since I started this project, thank-you for your continual support, advice and willingness to lend a hand.

My thanks also to Te Rōpū Rangahau Hauora a Eru Pōmare, at the Wellington School of Medicine and Health Sciences, for their ongoing interest in my work. I am also grateful for the support I have received from MAI ki Poneke, the Wellington branch of the National Programme for Māori and Indigenous Post-Graduate Advancement.

The PhD journey is often a lonely time, not just for the student, but also for our family and friends. My love and thanks to my family, for your unwavering belief in me, and for putting up with my obsession. Finally, to Laird, my thanks for the sacrifices you have made so I could finish this work, and for listening to me, even when I didn't have much to say.

Taku aroha ki a koutou katoa mō ake tonu atu

I would also like to acknowledge the following people for their vital contribution to this research programme:

This work was carried out during the tenure of a Māori Health PhD Scholarship from the Health Research Council of New Zealand (HRC 03/020).

Study One was funded by the Sleep/Wake Research Centre, at Massey University. My thanks to Noemie Travier for her excellent statistical support.

The recruitment of participants for Studies Two and Three was tirelessly undertaken by Michelle Gray. My thanks also to the doctors who agreed to carry-out the medical examinations. Funding for these studies was provided by a project grant from the Lotteries Health Board. Particular thanks to Noemie Travier, Margo van den Berg and Kara Mihaere for helping me with the overnight laboratory protocol conducted in Study Three. My thanks also to Associate Professor Dave Kennaway at the University of Adelaide, Australia, for his advice with regards to the study design, and also for the analysis of the saliva samples. The Centre for Public Health Research kindly allowed me the use of their laboratory facilities. Leigh Signal provided invaluable data management and statistical advice throughout these studies.

Ngā Pae o te Māramatanga (Horizons of Insight), The National Institute of Research Excellence for Māori Development and Advancement, provided funding for Study Four. My thanks to Papaarangi Reid and Fiona Cram for supporting me throughout this work and to Tamara Byrne, who provided valuable assistance during the focus groups.

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ABBREVIATIONS & TECHNICAL TERMS

95% CI	95% confidence interval
ACC	Accident Compensation Corporation
ActSlp	Actual sleep time
ActSlpP	Actual sleep time percentage
Allele	One of the different forms of a gene that can exist at a single locus
Amplitude	The difference between the maximum and minimum points of a biological rhythm
aMT6s	6-sulfatoxymelatonin; the urinary metabolite of melatonin
ANOVA	Analysis of Variance
ANCOVA	Analysis of Covariance
ASPS	Advanced Sleep Phase Syndrome
AssSlp	Assumed sleep time
AUC	Area under the curve
Autosomal dominant	An allele that masks the expression of another allele
BMI	Body Mass Index
BT	Bed Time
CBT	Core Body Temperature
Chromosome	A linear end-to-end arrangement of genes and other DNA, sometimes with associated proteints and DNA
Chronobiology	The study of biological clocks
Chronotype	A circadian phenotype
Circadian	Latin for '*about a day'*. Refers to self-sustaining rhythms which have a periodicity of approximately 24-hours
Constant Routine	A study design used to examine endogenous rhythms free of the masking effects of sleep, posture, activity, and meals
CRS	Contact record sheet
CT	Circadian time
DASS-21	The short form of the Depression, Anxiety, and Stress Scale (DASS)
DD	Dark/Dark cycle. Refers to the use of two dark periods within one cycle and is the experimental manipulation of constant conditions
DE-type	Definitely Evening-Type
df	Degrees of freedom
Dimerise	The chemical union of two identical molecules

Diurnal	Day-active
DLMO	The Dim Light Melatonin Onset
DLMO20%	The Dim Light Melatonin Onset defined as 20% of maximum melatonin concentration for that individual
DLMO25	The Dim Light Melatonin Onset defined as 25% of maximum melatonin concentration for that individual
DLMO50	The Dim Light Melatonin Onset defined as 50% of maximum melatonin concentration for that individual
DLMOff	The Dim Light Melatonin Offset
DLMOff25	The Dim Light Melatonin Offset defined as 25% of maximum melatonin concentration for that individual
DLMOff50	The Dim Light Melatonin Offset defined as 50% of maximum melatonin concentration for that individual
DM-type	Definitely morning-type
DNA	Deoxyribose nucleic acid
ECART	The Ethics Committee on Assisted Reproductive Technology
EEG	Electroencephalogram
EMG	Electromyogram
Entrainment	The process of synchonisation of a self-sustaining rhythm to the environmental light/dark cycle
EOG	Electrooculogram
Epoch	A measure of duration of a sleep measurement
ERMA	The Environmental Management Authority
ESS	The Epworth Sleepiness Scale
ESR	The Environmental Science and Research Limited
E-type	Evening-Type
F	F-statistic
False negative	The ratio of the number of events incorrectly classified as non-events over the sum of all observations classified as non-events
FASPS	Familial Advanced Sleep Phase Syndrome
FGP	Focus Group Participants
FragIn	Movement and Fragmentation Index

Free run	The state of a circadian rhythm under constant conditions (i.e. DD); A circadian rhythm that is not entrianed to zeitgebers and therefore is running at its endogenous period length
GATT	General Agreement on Tarriff and Trade
GE	Genetic Engineering
GM	Genetic Modificaiton
GUT	Get Up Time
Heterozygous	A gene pair having different alleles in both copies e.g. AA or aa
Homozygous	A gene pair having identical alleles in both copies e.g. AA or aa
HRC	The Health Research Council of New Zealand
Heterodimer	A complex of two different proteins
HIOM	Hydroxyindole-O-methyltransferase
HTIF	The Human Time Isolation Facility
HSNO	Hazardous Substances and New Organisms
HRCEC	The Health Research Council Ethics Committee
HUGO	The Human Genome Organisation
ICSD	The International Classification of Sleep Disorders
in vitro	Latin for '*in glass'*. An experimental situation ouside the organism
IQR	Interquartile Range
IVF	*in vitro* fertilisation
KI	Key-informant
Knock-out	The process of purposely removing a particular gene or trait from an organism
KMR	Kaupapa Māori Research
KSS	Karolinska Sleepiness Scale
K-W	Kruskal-Wallis test
LD	The light/dark cycle (i.e. a fixed schedule most commonly 12 hours light and 12 hours dark)
Linkage analysis	A mathematical procedure that analyses meiotic recombination frequencies between pairs of genes to determine whether two loci are linked and, if so, how closely
Locus	The position of a gene, DNA marker or genetic marker on a chromosome
Log10	Log to base 10
LOWESS	Locally Weighted Scatterplot Smooth

Lux	The measure of light intensity which is based on the spectural sensitivity distribution of rods and cones
MActSc	The Mean Activity Score
Masking	The concealment or alteration of a self-sustaining rhythm by environmental or behavioural factors (i.e. light, posture, meals, sleep)
MelStart	Melatonin Start Time. Represents the first detectable melatonin level
MelEnd	Melatonin End Time. Represents the last detectable melatonin level
MEQ	The Horne and Ostberg Morningness/Eveningness Questionnaire
MEQ1	MEQ scoring criteria developed by Horne and Ostberg (1976)
MEQ2	MEQ scoring criteria developed by Taillard and colleagues (2004)
Metazoan	An animal whose body consists of cells that are separated into different parts such as tissues and organs. All animals except for sponges and protozoans are classified as metazoans.
MOU	Memorandum of Understanding
mRNA	An RNA molecule transcribed from the DNA of a gene, and from which a protein is translated by the action of ribosomes. The basic funtion of the nucleotide sequence of mRNA is to determine the amino acid sequence
MSlpEff	Mean Sleep Efficiency
Mutation	The process producing a gene or a chromosome differing from the wild-type
NAT	*n*-acetyltransferase
NEAC	The National Ethics Advisory Committee
Night work	A pattern of work which involves working for at least 3 hours between midnight and 5am
NKTT	Nga Kaihautu Tikanga Taiao (The Māori Advisory Committee of ERMA)
non-REM	non-Rapid Eye Movement
Nucleotide	A subunit that polymerises into nucleic acids (DNA or RNA). Each nucleotide consists of a nitrogenous base, a sugar and one to three phosphate groups

Null allele	An allele whose effect is either an absence of normal gene product at the molecular level or an absence of normal function at the phenotypic level
NZDep	The New Zealand Deprivation Index
OR	Odds Ratio
Orthologous	Genes that have evolved directly from an ancestral gene
OSA	Obstructive Sleep Apnoea
OSAS	Obstructive Sleep Apnoea Syndrome
Period	The time interval between recurrances of a defined phase of a rhythm
pg/ml	picograms per millilitre
Phase	The position of the circadian clock in its cycle
Phase angle	The difference in time or degrees between the phase of one rhythm and the phase of another rhythm or environmental cycle
Phase advance	An earlier relative phase position
Phase delay	A later relative phase position
Phase marker	Any identifiable point in the cycle of a rhythm (e.g. maximum or minimum)
Phase shift	The process of moving the phase position of the circadian clock to an earlier (phase advance) or later (phase delay) clock time
Phenotype	The detectable outward manifestation of a specific genotype; the observable attributes of an organism
Phosphorylate	To add phosphate e.g. to a protein to alter its function
Photoperiod	The duration of light in a light/dark cycle
pM	picomolar units
Polymorphism	The occurance in a population (or among populations) of several phenotypic forms associated with alleles of one gene or homologues of one chromosome
Prevalence	The number of instances of a given disease or occurrence in a given population at a specific point in time
PRC	Phase Response Curve
PSG	Polysomnography, the gold standard measure of sleep consisting of EEG, EOG and EMG channels
PSQI	The Pittsburgh Sleep Quality Index

***p*-value**	A statement of the probability that the difference observed could have occurred by chance, reflecting the statistical significance of the result
PVT	The Psychomotor Vigilance Task
r	Correlation coefficient
REM	Rapid Eye Movement
RCoGM	The Royal Commission on Genetic Modification
RNA	Ribonucleic acid
RR	Response Rate
REML	Residual Maximum Likelihood estimation
RIA	Radioimmunoassay
SBC	Schwarz-Bayesian Criteria
SCN	Suprachiasmatic Nucleus
SD	Standard Deviation
Shift work	Any work that forces sleep to be displaced
SlpEff	Sleep Efficiency
SlpEnd	Sleep End Time
SlpSt	Sleep Start Time
SNP	Single Nucleotide Polymorphism; DNA sequce variation that occurs when a single nucleotide (A, T, C, or G) in the genome sequence is altered
SQRT	Square Root Transformation
Subjective day	The light portion of the LD cycle for diurnal species and the dark portion of the LD cycle for nocturnal species
Subjective night	The dark portion of the LD cycle for diurnal species and the light portion of the LD cycle for nocturnal species
S-W	Shapiro-Wilk Test
SWA	Slow Wave Activity
SWRC	The Sleep/Wake Research Centre
SWS	Slow Wave Sleep
TActSlp	Total Actual Sleep Time
TAssSlp	Total Assumed Sleep Time
TIB	Time in Bed
TMActSc	Total Mean Activity Score
TMFragIn	Total Movement and Fragmentation Indec
t	The *t*-statistic
$\mathbf{T_{min}}$	The minimum of the core body temperture rhythm
Transactivation	The stimulation of transcription by a transcription factor binding to DNA and activating adjacent proteins

Transcription	The process whereby RNA is synthesised from a DNA template
Transcription factor	A protein that binds to a cis-regulatory elements and thereby, directly or indirectly, affects the initiation of transcription
Translation	The process of protein synthesis whereby the primary structure of the protein is determined by the nucleotide sequence in mRNA
The Treaty of Waitangi	The founding document of New Zealand signed in 1840 by some Māori chiefs and representatives of the Crown
TTiB	Total Time in Bed
Wild-type	A strain or characteristic which prevails in natural conditions, as distinct from an atypical mutant
WTO	The World Trade Organisation
x^2	Chi-square
Y=a+b*X	The regression equation. The Y variable can be expressed in terms of a constant (a) and a slope (b) times the X variable. The constant is also referred to as the intercept, and the slope as the regression coefficient or B coefficient.
Zeitgeber	German for *time giver*. External stimuli that provide time cues for the synchronisation of the circadian clock
ZT	Zeitgeber Time

MĀORI TERMS

Aotearoa	New Zealand; the land of the long white cloud
Aroha	Love
Atua	Gods, deity
Ea	The successful restoration of relationships
Hapū	Sub-tribe
Hawaaiki	Ancestral homeland
Hinengaro	Psyche; the mental state
Hine-nui-te-Pō	Originally named Hinetītama; in Māori mythology she is the great woman of the place of the departed spirits
Hui	Gathering
Iwi	Tribe
Ira tangata	Human element; gene
Kai	Food
Kanohi kitea	The face seen
Kainga	Home
Kaitiaki	Guardian
Kaitiakitanga	Guardianship
Kaupapa	Foundation; base; philosophy
Kaumatua	Elder
Kawa	Protocol
Mana	Authority; presitge; power
Manaakitanga	Hospitality; an expected state of behaviour
Mana motuhake	Separate authority; effective outcomes and evidence of benefit
Mana tangata	Dignity; safety; mutuality
Mana whakahaere	Collaboration; control
Mana whenua	The tribe who hold the authority of the area
Manuhiri	Guests
Marae	A complex of buildings and the surrounding land; a focal point for a sub-tribe
Mataatua	Māori for *'the face of god'*; one of the canoe which brought Māori to Aotearoa/New Zealand
Mātauranga	Knowledge
Maui	A special force within Māori mythology who was responsible for many great feats including the fishing up of the North Island of Aotearoa/New Zealand
Mauri	Life essence
Mihimihi	Greeting

Ngā Wahine Tiaki o te Ao	Guardians of our world; a group of Māori women concerned with genetic engineering and the future of our world
Ngāti Kahungunu	The tribe located in Hawkes Bay to Wairarapa
Nga Kaihautu Tikanga Taiao	The Māori Advisory Committee of the Environmental Risk Management Authority
Ngāti Porou	The tribe located on the East Coast of the North Island
Ngāti Rongo	A sub-tribe of Tūhoe
Ngai Tahu	The tribe located in the South Island
Noa	The restoration of balance
Pākehā	Person of predominately European descent; not Māori
Pono	True; genuine
Powhiri	The traditional practice of welcoming guests
Rangatahi	Youth
Rangatira	Chief; noble status
Ranginui	The sky father; a god personified in the sky
Rongoa Māori	Traditional medicine and healing practices
Rongokarae	The ancestor of the Ngāti Rongo hapū of Tūhoe
Ruatoki	Settlement in Te Urewera
Tangata whenua	People of the land; indigenous people
Tane	Man
Tāne	Men
Taonga	A treasured possession
Tapu	Sacred
Tauarau	The marae belonging to the Ngāti Rongo hapū of Tūhoe
Tauranga-Moana	Tauranga, Bay of Plenty
Te ao marama	Māori for *'the world of light'*
Te ao Māori	The Māori world
Te ao turoa	The natural world
Te hohonutanga	In depth
Te Kopere	The Māori Caucus of the Constructive Conversations Project
Te Mahurehure	A sub-tribe of Tūhoe
Te maramatanga	Understanding; enlightenment
Te reo	The Māori language
Te Pumanawa Hauora	The Māori Health Research Centre at Massey University
Te Rōpū Rangahau Hauora a Eru Pōmare	The Eru Pōmare Māori Health Research Centre at the Wellington School of Medicine and Health Sciences

Te Runanga o Ngai Tahu	The Ngai Tahu tribal authority
Te Ture Whenua Act	The Māori Land Act
Te Urewera	Lands belonging to the Tūhoe people
Te Whakatane	A sub-tribe of Tūhoe
Te whanuitanga	Outwards
Tiaki	Guard; protect
Tika	Right; correct
Tikanga	Cultural practices
Tinana	Body
Tino rangatiratanga	Self-determination; sovereignty; absolute chieftenship
Tipuna	Ancestor
Tūhoe	The tribe of Te Urewera
Wahine	Woman
Wāhine	Women
Waikaremoana	Māori for *'the sea of rippling waters'*; a lake in Te Urewera
Wairoa	Town, Hawkes Bay
Wānanga	Schools of learning; discussions
Waka	Canoe
Whāngai	Foster child
Wairua	Spiritual essence
Whakapapa	Genealogy
Whakatane	City, Bay of Plenty. Landing place of the Mataatua waka
Whānau	Family; extended family
Whānaungatanga	Expressions of support; love within a family
Utu	Compensation; revenge; reciprocity