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# 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

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.

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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)

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

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-typeDNA 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-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

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 Modification

**GUT** Get Up Time

Free run

**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

HeterodimerA complex of two different proteinsHIOMHydroxyindole-O-methyltransferaseHTIFThe 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 RangeIVF in vitro fertilisationKI Key-informant

**Knock-out** The process of purposely removing a particular gene or trait from an

organism

KMR Kaupapa Māori ResearchKSS 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)

A mathematical procedure that analyses meiotic recombination

**Linkage analysis** 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

The measure of light intensity which is based on the spectural sensitivity Lux

distribution of rods and cones

MActSc The Mean Activity Score

The concealment or alteration of a self-sustaining rhythm by Masking

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)

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

Metazoan

**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

The process producing a gene or a chromosome differing from the wild-Mutation

type

**NAT** *n*-acetyltransferase

**NEAC** The National Ethics Advisory Committee

A pattern of work which involves working for at least 3 hours between Night work

midnight and 5am

Nga Kaihautu Tikanga Taiao (The Māori Advisory Committee of **NKTT** 

ERMA)

non-Rapid Eye Movement non-REM

A subunit that polymerises into nucleic acids (DNA or RNA). Each Nucleotide

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

The occurance in a population (or among populations) of several

**Polymorphism** 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

A statement of the probability that the difference observed could have *p*-value

occurred by chance, reflecting the statistical significance of the result

**PVT** The Psychomotor Vigilance Task

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

Any work that forces sleep to be displaced Shift work

**SlpEff** Sleep Efficiency **SlpEnd** Sleep End Time **SlpSt** Sleep Start Time

Single Nucleotide Polymorphism; DNA sequee variation that occurs

**SNP** when a single nucleotide (A, T, C, or G) in the genome sequence is

altered

**SQRT Square Root Transformation** 

The light portion of the LD cycle for diurnal species and the dark portion Subjective day

of the LD cycle for nocturnal species

The dark portion of the LD cycle for diurnal species and the light portion **Subjective night** 

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

Total Actual Sleep Time **TActSlp** Total Assumed Sleep Time **TAssSlp** 

TIB Time in Bed

**TMActSc** Total Mean Activity Score

Total Movement and Fragmentation Indec **TMFragIn** 

t The *t*-statistic

The minimum of the core body temperture rhythm  $T_{min}$ 

The stimulation of transcription by a transcription factor binding to DNA Transactivation

and activating adjacent proteins

The process whereby RNA is synthesised from a DNA template **Transcription** 

**Transcription** factor

A protein that binds to a cis-regulatory elements and thereby, directly or indirectly, affects the initiation of transcription

The process of protein synthesis whereby the primary structure of the **Translation** 

protein is determined by the nucleotide sequence in mRNA

The Treaty of Waitangi

Y=a+b\*X

The founding document of New Zealand signed in 1840 by some Māori

chiefs and representatives of the Crown

TTiB Total Time in Bed

A strain or characteristic which prevails in natural conditions, as distinct Wild-type

from an atypical mutant

WTO The World Trade Organisation

 $\mathbf{x}^2$ Chi-square

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.

German for time giver. External stimuli that provide time cues for the Zeitgeber

synchronisation of the circadian clock

Zeitgeber Time  $\mathbf{Z}\mathbf{T}$ 

## **MĀORI TERMS**

New Zealand; the land of the long white cloud Aotearoa

Aroha Love

Gods, deity Atua

The successful restoration of relationships Ea

Hapū Sub-tribe

Ancestral homeland Hawaaiki Psyche; the mental state Hinengaro

Originally named Hinetītama; in Māori mythology she is the great Hine-nui-te-Pō

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

Foundation; base; philosophy Kaupapa

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

Dignity; safety; mutuality Mana tangata

Mana

Maui

Collaboration; control whakahaere

The tribe who hold the authority of the area Mana whenua

Manuhiri Guests

A complex of buildings and the surrounding land; a focal point for a Marae

sub-tribe

Māori for 'the face of god'; one of the canoe which brought Māori to Mataatua

Aotearoa/New Zealand

Mātauranga Knowledge

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

Life essence Mauri 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 The Māori Advisory Committee of the Environmental Risk

**Tikanga Taiao** 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-MoanaTauranga, Bay of PlentyTe ao maramaMāori 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

The Māori Health Research Centre at Massey University

Te Rōpū

Rangahau Hauora

a Eru Pomare

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