

SALIVARY DLMO CIRCADIAN PROFILE

Clarify underlying etiology and characterize the nature of sleep disorders with a reliable index of circadian timing for research, diagnosis and effective treatment of circadian rhythm sleep disorders (CRSD).

WHAT IS A CIRCADIAN PROFILE?

A profile of Melatonin secretion, using only a few drops of saliva, can characterize an individual's circadian rhythm and reveal phase discrepancies from a normal sleep pattern. A DLMO (Dim Light Melatonin Onset) Circadian Profile is a useful tool in academic and clinical studies involving circadian rhythm sleep disorders. Many sleep disorders have been implicated in the exacerbation of life threatening diseases such as heart disease, obesity, hypertension, cancer, stroke and depression.

WHAT IS MELATONIN?

Melatonin, a sleep-promoting neurohormone, is responsible for the entrainment of circadian rhythm. The pineal gland produces Melatonin in response to light/dark stimulation. Circadian rhythm is also modulated by environmental cues including bright light, diet, social behavior and exercise.

Melatonin secretion begins at approximately 2 hours before habitual bedtime, peaks in the middle of the night (2-4 am) and drops to minimal levels during the day (nadir in late afternoon).

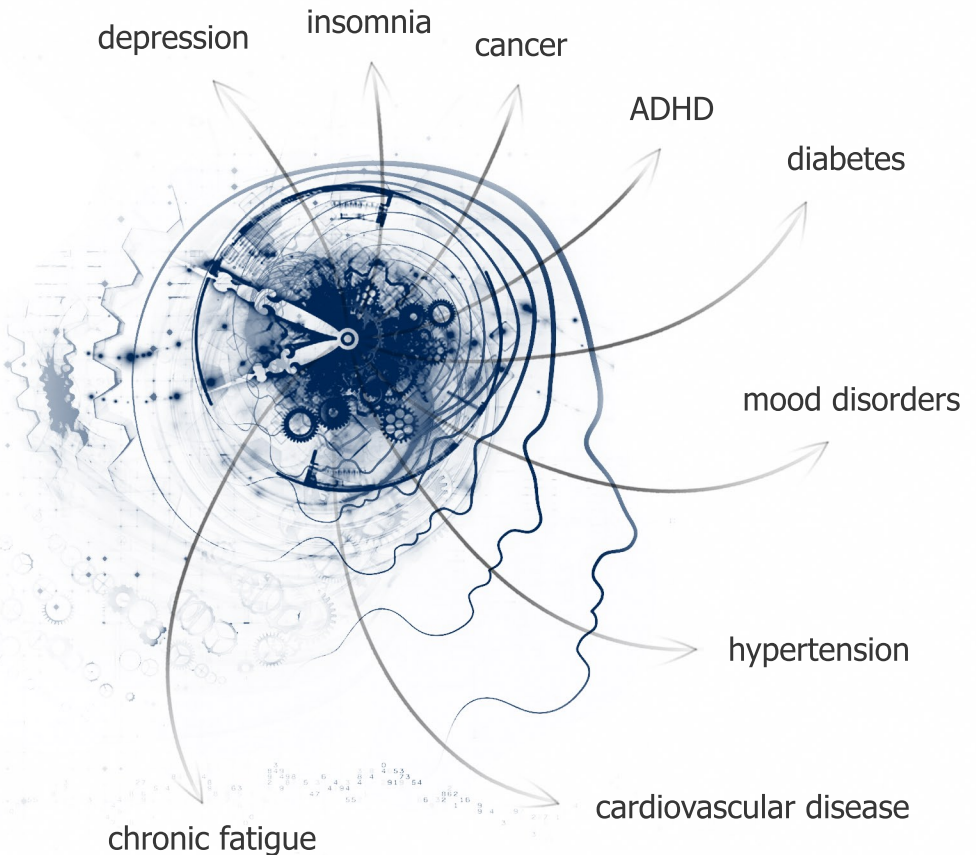
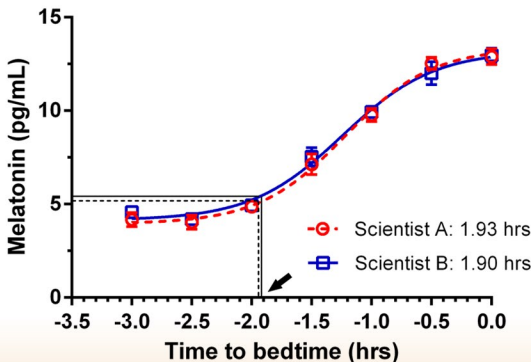


FIGURE 1:
Example DLMO Determination



WHAT'S CIRCADIAN RHYTHM?

A normal body clock (circadian rhythm), functions on a 24 hour cycle and allows organisms to anticipate and prepare for environmental changes. Irregular circadian sleep patterns result in poor concentration, memory, decreased productivity at work or school, and poor athletic performance. These patterns may be the result of behavior or sleep disorders which can result in a sleep/wake cycle shift leading to insufficient sleep. Trying to force a "normal sleep schedule" on a person with a delayed or advanced sleep phase shift often results in a chronic sleep deficit, producing symptoms that can be confused with psychophysiological insomnia, depression, schizophrenia, ADHD, fibromyalgia, chronic fatigue and/or school refusal.

WHAT IS DLMO?

The initiation of Melatonin production, referred to as "Dim Light Melatonin Onset" (DLMO), is the most reliable parameter to assess an individual's circadian rhythm pattern and is used to diagnose circadian rhythm sleep problems. DLMO is a time point in which circulating Melatonin has risen two standard deviations above the low baseline concentrations present during the day. **Figure 1** shows representative DLMO determination data using the Salimetrics Salivary Melatonin Assay. To illustrate assay precision and reproducibility, data is shown for samples run by two different scientists, tested in duplicate with error bars shown.

CIRCADIAN RHYTHM SLEEP DISORDERS:

Abnormally shifted Melatonin secretion to later in the night results in a circadian rhythm sleep disorder termed "Delayed Sleep Phase Disorder (DSPD)". Symptoms include extreme difficulty in initiating sleep at a conventional hour (chronic sleep onset insomnia) and difficulty waking at a conventional hour leading to chronic sleep deprivation, daytime sleepiness and fatigue. Prevalence is less than 1% in adults and up to 16% in adolescents. Conversely, if melatonin secretion starts too early, the result is Advanced Sleep Phase Disorder (ASPD). Symptoms are severe sleepiness in the early evening and very early morning awakenings with the inability to go back to sleep. Roughly 1% of the middle age and older population experience ASPD. Chronic disruption in the circadian rhythm results in sleep disorders that can cause chronic illnesses.

SAMPLE TIMELINE:

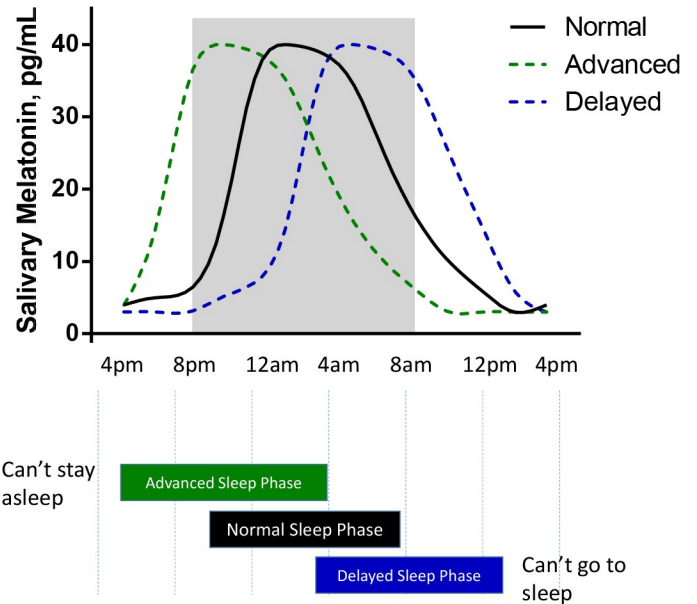
(Normal Bedtime)

Time	7pm	8pm	9pm	10pm	11pm			
Habitual Sleep Time (HRS)	-4	-3	-2	-1	0			
Samples		1	2	3	4	5	6	7

HOW DOES IT WORK?

- 1 Study participant/Patient contact and "Salimetrics DLMO Circadian Profile" ordered
- 2 Participant receives saliva collection kit containing:
 - a. Labeled collection vials/Saliva Collection Aids
 - b. Storage box
 - c. Instructions
 - d. Shipping container/ice packs
- 3 Patients choice of evening (in the convenience of home)
 - a. 3 hours before habitual sleep time (determined by a sleep diary for 1 week prior)
 - Sample collection – 7 samples total (every 30 minutes) (dim light, no electronics, certain dietary restriction for day of testing)
 - b. Samples shipped with ice to SalivaLab directly
 - c. Results sent to researcher or clinician (Graphical data provided for ease of diagnosis)
 - d. Personalized therapy prescribed

FIGURE 2: Example Sleep Phase Shifts



A FEW DROPS OF SALIVA?

Monitoring melatonin levels can be as easy as collecting saliva samples from participants in the comfort of their own home (within a 3 hour period), eliminating the need of an overnight clinic stay for a polysomnogram (up to 12 hours). This also eliminates any rhythm perturbation caused by the clinical sleep center setting. Samples are collected every 30 min for 3 hours, stored in a freezer, and then delivered to the laboratory for Melatonin testing.

The resultant calculated Phase Response Curve (see example of results in **Figure 2**) provided to the researcher/clinician, tracks the rise in salivary Melatonin and the DLMO value. In this easy to read format, phase shifts away from the norm are readily detected, enabling proper diagnosis. With an accurate DLMO, critical timing of therapy can be optimized for the individual and increase the rate of treatment success.

SAMPLE COLLECTION KIT

