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A Dynamic Model of Circadian Rhythm of Melatonin and the Effect of Night Shifts on Risk of Autism in Late-Stage Pregnancy

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INTRODUCTION

Melatonin, known as the hormone of darkness, is a hormone that has a circadian clock and protects the body against oxidative stress with its antioxidant properties. Maternal melatonin production and melatonin circadian rhythm are disrupted by light exposure during the night due to night shift work, which affects fetal brain development through increased oxidative stress markers such as Malondialdehyde (a marker of oxidative stress).

Autism spectrum disorder (ASD) is a neurodegenerative disorder and in recent years, an increase in the prevalence of autism has been observed. A study conducted on mothers of children with autism has found that melatonin levels are approximately 40 percent lower than the age-adjusted melatonin levels in mothers of children without autism [1].

GOAL

The study aims to model the dynamic effects and causal interactions of disruption of the melatonin rhythm of a pregnant woman (third trimester of pregnancy) working the night shift on the melatonin and Malondialdehyde rhythms of the fetus and the risk of autism in the fetus.

METHOD

A simulation model of maternal-fetal circadian rhythm disruption and its impact on autism risk is constructed.

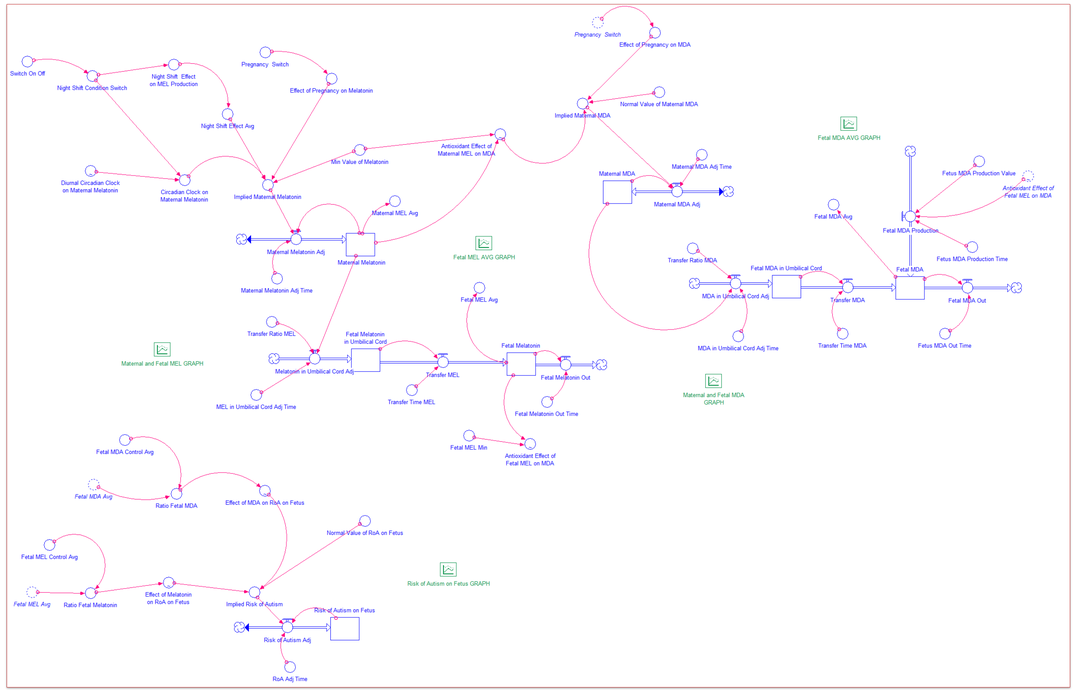
The system boundaries of the problem suggest two interconnected subsystems: the maternal-fetal melatonin circadian rhythms and the maternal-fetal MDA (oxidative stress) circadian rhythms. Healthy maternal circadian and disrupted maternal circadian patterns (due to night shift work) are determined, and interactions between maternal and fetal variables are defined based on the literature. Stella modeling and simulation software version 10.0.6 is used for model construction and simulations.

In scenario analysis, different night shift work conditions are simulated.

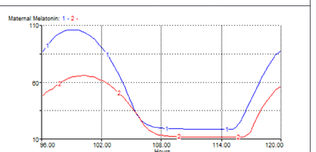
Experiments:

	Night Shift Condition
Experiment Base Run	4 nights of work followed by 3 days off
Experiment 1	5 nights of work followed by 2 days off
Experiment 2	3 nights of work followed by 4 days off
Experiment 3 (Extreme Condition)	2 nights of work followed by 5 days off
Experiment 4	Base experiment quitting the night shift after 1.5 months

RESULTS

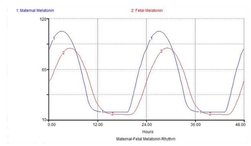
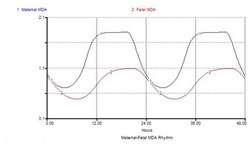
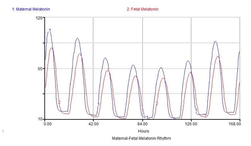
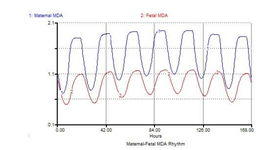


Melatonin Circadian Clock in Shift Workers: Day vs. Night

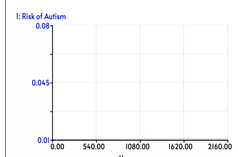
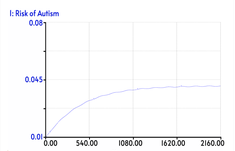
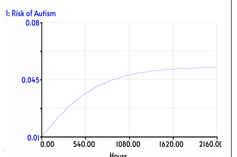
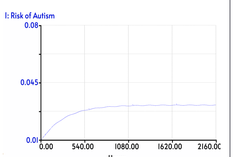
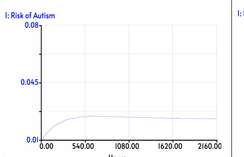
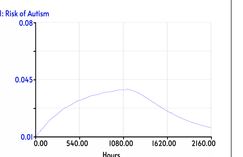


A study on Danish nurses found that working night shifts leads to lower melatonin levels because of constant light exposure. Even on their days off, night shift nurses still had lower levels than those working during the day, although the difference was smaller. [2]

The simulation results align with with [3] in terms of acrophase and dynamics, though the peak time differs, matching that reported by [4].

Control Melatonin Levels	Control Malondialdehyde Levels	Base Experiment Melatonin Levels	Base Experiment Malondialdehyde Levels
			

Risk of Autism

Control	Base	Exp. #1	Exp. #2	Exp. #3 (Extreme Condition)	Exp.#4 (Quitting Night Shift)
					
0.01	0.041	0.052	0.031	0.023	0.015

CONCLUSIONS

Limited data exists on fetal circadian rhythms or maternal melatonin transfer to fetus.

This is an initial simulation modeling study to understand the neurodevelopmental disorders that night shift work may cause in the fetus.

Night shifts reduce fetal melatonin levels by 22% and increase fetal malondialdehyde by 11%, significantly raising the risk of autism.

These findings suggest that night shift work during pregnancy increases the risk of autism in the fetus due to disruption of melatonin production and the resulting in increase malondialdehyde level.

Reducing these effects can lower the risk of autism highlighting the importance of managing oxidative stress and melatonin disruption.

Ending the night shift after some time reduces the risk of autism, but it never returns the risk of autism to the base level.

Considering these findings, the impacts of circadian disorders should be examined in more detail, and further clinical studies should be conducted on fetal health.

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