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Investigating light sensitivity in bipolar disorder (HELIOS-BD)

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Background

Circadian dysregulation in Bipolar Disorder (BD)

Many people with bipolar disorder have disrupted circadian rhythms. This means that the timing of sleep and wake activities becomes out-of-sync with the standard 24-hour cycle.

Many clinical features of bipolar disorder can be understood as circadian dysregulations [1], including:

- extreme mood changes
- disrupted sleep and wake schedules
- energy level fluctuations

Research also shows that levels of the circadian hormone melatonin change according to the bipolar disorder mood state (euthymic/ depressed/ (hypo)manic) [2].

Light hypersensitivity hypothesis

Many people with BD exhibit:

- Mood shifts in line with the seasons (manic in spring/summer, depressed in autumn/winter) [3]
- Increased melatonin suppression in response to light [4]
- Increased light-induced phase delays [5]

This suggests people with BD have a hypersensitivity to light, which could in turn lead to dysregulation of circadian rhythms. It is likely this light hypersensitivity is due to changes to a type of retinal cell called 'melanopsin-expressing intrinsically photoreceptive retinal ganglion cells' (ipRGCs) [6].

It is not known how this light sensitivity relates to other changes in retinal structure and function.

A potential mechanism of action for Lithium

Lithium is the gold-standard treatment for bipolar disorder, yet the mechanism of action is unclear.

One potential mechanism of action for Lithium is by regulating circadian rhythmicity by inhibiting cellular signalling pathways including glycogen synthase kinase-3β (GSK-3β) [7] and protein kinase C [8].

One therapeutic effect of lithium may therefore be dampening light hypersensitivity in bipolar disorder [9], ultimately resulting in stabilisation of circadian rhythms.

Hypotheses

1. People with bipolar disorder have a hypersensitivity to the visual and non-visual effects of light, causing light-induced circadian rhythm disruption
2. Bipolar disorder light hypersensitivity is caused by retinal microstructural changes
3. Lithium is effective in bipolar disorder because it reduces retinal hypersensitivity to evening light

Study design

We are investigating the light hypersensitivity hypothesis of bipolar disorder in an experimental study with cross-sectional and longitudinal data collection from three participant groups. Over an 18-month period, participants attend multiple study visits to complete a range of tests, from retinal imaging to electrophysiological recordings and melatonin suppression experiments.

All HELIOS-BD study activities, from research design to results analysis and communication of results, are done in collaboration with people with lived experience of bipolar disorder, as part of our HELIOS-BD Lived Experience Advisory Panel (LEAP).

Recruitment partners

Recruitment is **Scotland-wide**

- Bipolar Scotland
- NRS Mental Health Network
- Scottish Health Research Register and Biobank
- NHS Scotland PIC sites
- HELIOS-BD Bipolar Disorder Lived Experience Advisory Panel (LEAP)

RECRUITMENT BEGAN JANUARY 2024

Participants

3 groups of participants

- People with bipolar disorder taking lithium (n=60)
- People with bipolar disorder **not** taking lithium (n=60)
- People without bipolar disorder (controls) (n=60)

Participation Schedule

Participants complete 6 study visits over 18 months

Month: 0

Baseline study visit
- Demographics
- Medical History
- Function
- Sleep profile
- Circadian profile

Retinal imaging (baseline)
- Structural and functional retinal imaging

(e.g. OCT, OCT-angiography, fundus photography, automated perimetry, optical biometry)

Overnight melatonin suppression experiments
- 2x overnight sleep studies
- Melatonin profile (hourly)
- Night-time light stimulation to assess melatonin suppression

Functional retinal assessments
- Visually-evoked potentials (EEG)
- Pupilometry
- Colour psychophysics experiments

Month: 9

Retinal imaging (follow up)
- Structural and functional retinal imaging

Month: 18

Retinal imaging (follow up)
- Structural and functional retinal imaging

How you can help

We would be grateful if you could consider helping us in our continuing recruitment of participants with bipolar disorder, for example by:

- Directing patients and colleagues to our website heliosbd.com/take-part
- Distributing informational materials: our participant information sheet, study information sheet and study poster can be found on our website. Please get in touch with us if you would like us to send printed copies to you
- Asking us to attend team meetings or teaching sessions to speak about the study

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Summary

HELIOS-BD tests an important and still unresolved hypothesis on bipolar disorder light hypersensitivity and the mechanism of action of lithium at both cellular and systems levels. The project has considerable translational potential and will further our understanding of bipolar disorder pathophysiology. Most importantly, HELIOS-BD centers the experience of people with BD, making sure the research reflects their views and experiences. We are currently in the process of recruiting participants from across Scotland, with the aid of our recruitment partners and clinical colleagues.

Acknowledgements

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