Study protocol: a cross-sectional survey of seasonal affective disorder in Danish populations with and without severe visual impairments

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ABSTRACT

Introduction: People with seasonal affective disorder (SAD) experience recurrent seasonal fluctuations in energy, mood and appetite. Retinal light exposure is suggested to play an important role in the pathogenesis and treatment of SAD. The aim of the study is to determine the prevalence of SAD in persons with severe visual impairments or blindness and to compare the results to a control group without visual impairments. Moreover, the authors wish to investigate whether SAD is correlated to the degree of impairment or to the diagnosis.

Methods and analysis: 2781 persons with visual impairments ranging from total blindness to Snellen visual acuity 6/60 receive information letter and questionnaire by post. Completed questionnaires can be returned by post, email or telephone. For each respondent, all eye-related diagnoses will be obtained from national registries. Normally sighted and demographically matched control respondents will be contacted in a similar manner the subsequent winter season. The Seasonal Pattern Assessment Questionnaire rates seasonal variation within the six items: sleep, appetite, social activity, mood, energy and body weight. The Seasonal Pattern Assessment Questionnaire yields a Global Seasonal Score and a prevalence of SAD. Outcomes from the two groups will be compared. Moreover, outcomes from subgroups of the visually impaired population will be compared.

Ethics and dissemination: The study is approved by the Danish Data Protection Agency. Results will be published in a relevant scientific journal and be communicated to respondents and relevant institutions through cooperation with the Danish Association of the Blind.

INTRODUCTION

Seasonal affective disorder (SAD) or winter depression is a syndrome of seasonally occurring reductions in mood, energy and social initiative along with increases in appetite, body weight and sleep duration. The effectiveness of light therapy in the treatment of SAD was established in a 2005 meta-analysis reporting effect sizes of 0.84 (CI 0.60 to 1.08) for bright white light and 0.73 (CI 0.37 to 1.08) for dawn simulation, the two most prominent types of light therapy. Merely ocular, not cutaneous, exposure is effective in alleviating symptoms. On this background, it is assumed likely that diminished retinal light exposure plays a significant role in the development of each case of SAD.

For SAD patients, photoperiod (day length), hours of sunshine and global radiation are the strongest climatic predictors for onset of disease. However, the suggested correlation between SAD prevalence and latitude of living only receives weak support from published meta-analysis. The

ARTICLE SUMMARY

Article focus
- The prevalence of SAD in a visually impaired population.
- The prevalence of SAD correlated to degree of visual impairment or type of impairment.

Key messages
- Any association between visual impairment and SAD will add to current knowledge of the role of retinal light exposure in the development of SAD.
- The occurrence of SAD in visually impaired populations is a previously uninvestigated area that may hold non-pharmacological therapeutic potential to many people.

Strengths and limitations of this study
- Through use of the vast national registries of the Danish Health System and our cooperation with a major Danish organisation for blind and visually impaired persons, we have unique access to a large identifiable study population with visual impairment.
- The applied questionnaire has undergone widespread use allowing for comparisons between many different populations despite its diagnostic limitations.

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association between SAD and melatonergic disturbances remains unclear. A single study has found an increase in the duration of nocturnal melatonin secretion in male SAD patients compared with healthy controls. The phase shift hypothesis suggests that SAD is caused by a fall/winter delay in circadian rhythms. Approximately 50% of SAD patients seem to exhibit a shift in the evening onset of melatonin secretion compared with healthy controls. This shift can be corrected by properly timed light therapy. Some studies have even found an association between the degree of phase correction obtained by light therapy and the concurrent reduction in depressive symptoms, but the causal relation between these factors remain unresolved.

The overall retinal electrical response to light, measured by electrooculographic ratio, is found reduced in some studies of SAD patients. Other trials examining different measures of retinal status have yielded diverging and non-conclusive results.

Light can effectively suppress melatonin secretion in blind individuals with no conscious light perception (NLP) through newly identified pathways of the non-image-forming visual system, for example, melanopsin-containing intrinsically photosensitive retinal ganglion cells. The photopigment, melanopsin, demonstrates a peak spectral sensitivity to light with wavelengths of 460 nm, which is blue light. In new light therapy studies of SAD, blue light appears to be as effective as bright white light, suggesting an involvement of the melanopsin-dependent pathways in the treatment. Preliminary investigations have found associations between SAD and a mutated variant of the melanopsin gene, but reproduction of this finding is warranted.

Sleep disorders are a frequent complaint in NLP individuals, particularly in persons who have had one or both eyes removed. Blind adolescents with optical nerve damage (eg, glaucoma, diabetic retinopathy) are more prone to circadian disturbances than controls with other eye conditions.

Seasonal mood and energy variation is a common complaint in the northern hemisphere with SAD being the endpoint of a vast continuum. Screening studies from the Northern countries report prevalence estimates ranging from 3% to 12%. Traditionally, the syndrome has not been considered as disabling as classical depression, but during symptomatic episodes, SAD patients report reductions in quality of life equal to those experienced by individuals with classical major depressive disorder. On this background of a commonly occurring phenomenon with unclarified pathogenetic relations, we designed a survey to investigate the prevalence of SAD in a population with severe visual impairments or total blindness.

OBJECTIVES
The study has fourfold aims:

a. to determine SAD prevalence and extent of symptomatology in a Danish population of blind and visually impaired persons,

b. to compare the findings to a control group without visual impairments matched on gender, age and residential area,

c. to clarify whether SAD prevalence and extent of symptomatology correlate to the degree of visual impairment (light perception vs no light perception) and

d. to investigate whether SAD prevalence and the extent of symptomatology correlate to the type of visual impairment (anatomic localisation, congenital or acquired genesis).

METHODS
Design and setting
The study is a cross-sectional survey investigating the prevalence and symptomatology of SAD in a primary study population with severe visual impairments or total blindness compared with a sighted control population. The two surveys (study and control population) will be undertaken during consecutive winter seasons.

For all rounds of data collection, a similar methodology and time schedule will be applied. Postal send-outs are scheduled in October/November followed by a 1- to 2-months response period before starting a follow-up round of telephone interviews that extends into the subsequent year. Non-responders are attemptedly contacted by telephone on one to three separate occasions if a relevant telephone number can be attained.

Participants
Study population
All 2781 members of the Danish Association of the Blind (DAB) between 18 and 65 years of age are invited to participate in the study. DAB is an independent private organisation with approximately 12 000 blind and visually impaired members, corresponding to 50% of all blind and visually impaired persons in Denmark. Membership requires corrected sight equal to or less than Snellen visual acuity 6/60 in the eye with better vision. The vision loss must be documented by an ophthalmologist.

Prior to the study, a notice of the study is given in the DAB membership journal. Consequently, all members receive a normal print information letter and questionnaire along with a copy in either enlarged print (font Arial, size 18), braille font, audio disc or email. Questionnaire table items are transformed into single questions to avoid the obstacle of ticking off answers. Production of accessible means of information for visually impaired persons is obtained by advise from the DAB.

A prepaid return envelope is enclosed within all send-outs. Completed questionnaires can be returned by post or email. In addition, a contact telephone number is provided, and the research group is available for telephone interviews on all weekdays. If no answer is returned by post or email within 2 months, the member is contacted by telephone.
Control population
A control group is identified through the Danish Civil Registration System where all Danish citizens are registered by personal social security number. The control group is matched to the study population on important demographic variables: gender, age and residential area (postal code). Telephone numbers are obtained from a private telephone register (Eniro). To ensure that controls do not suffer severe visual impairments, the questionnaire contains a question regarding potential eye conditions.

Outcomes
Demographic variables
Respondents are asked to fill out name, gender, age and postal code. Study respondents are asked to fill out their social security number. If controls wish to answer anonymously, they can omit stating their name. If study respondents wish to answer anonymously, their data are only used for analysis of aim (a), (b) and (c) since their diagnosis thus cannot be attained from the registers.

Degree of visual impairment
To assess the respondents’ degree of visual impairment, the questionnaire sent to the study population contains three questions regarding the ability to detect light, to determine source and direction of light or to count fingers at a distance of 1 m from the eyes. These questions were conferred with the board of DAB before adding them to the questionnaire.

On the basis of the questionnaire replies, the study population can be divided into four groups according to degree of visual impairment.

Type of visual impairment
For each respondent in the study group, all registered relevant eye-related diagnoses and surgical procedures including date of contact to the hospital are obtained from the Danish National Patient Registry (table 1). The register contains data (date, hospital, diagnosis, treatment actions, etc.) of all contacts made to the public medical system identifiable through social security number. Diagnoses will be categorised according to genesis (congenital or acquired) and to anatomical localisation.

From 1977 to 1993, a different set of registration codes was used in the Danish Medical System. Records from these years are searched by their corresponding codes.

Seasonal variation
To evaluate self-reported seasonal variation, an existing Danish translation of The Seasonal Pattern Assessment Questionnaire (SPAQ) is used. The main component of SPAQ is a six-item scale where the respondent rates the variation he/she experiences across the seasons. The six items (sleep duration, social activity, mood, appetite, weight and energy) are each rated from 0 to 4 points. The sum score yields the Global Seasonal Score (GSS) of a maximum of 24 points. In addition, the respondent must rate to which extent the variation constitutes a problem and state during which months he/she feels worst. The cut-off score for SAD was originally set by Kasper et al at 11 or higher. Moreover, the variation has to constitute at least a moderate problem and the respondent must feel worst in a winter month (November, December, January, February). The SPAQ also defines a milder form of seasonal malaise, subsyndromal seasonal affective disorder (ssSAD). Two SPAQ definitions of ssSAD exist: (a) GSS ≥ 10 and the variation rated as no or only a mild problem or (b) GSS of 8 or 9 with the problem rated as at least a mild problem.6

The SPAQ has been widely used in epidemiological studies on SAD. The questionnaire does not have the properties of a diagnostic tool but is validated for use as a screening instrument. Its clinical validity has been discussed in recent years but its brief and simple construction and widespread use make it suitable for epidemiological research.22

Bias
Non-response
There may be a tendency that people are more inclined to answer the questionnaire if they are familiar with the current subject/suffer from the investigated condition. This situation will inflate the prevalence estimate found in our sample in case of substantial non-response. We attempt to evade this problem by informing the respondents of their value to the study even though they do not experience seasonal variation. Moreover, a comprehensive effort is put into follow-up by contacting as many as possible by telephone and offering them a short telephone interview. The estimates from the two populations can be correctly compared even if they do not reflect the actual prevalence of SAD.

Recall bias
Due to the fact that we exclusively contact each respondent at one occasion, there is a risk that respondents

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**Table 1 Data from the Danish National Patient Registry according to Sundhedsvæsenets Klassifikations System (SKS classification)**

| ICD code of diseases | Corresponding diagnosis                      |
|----------------------|----------------------------------------------|
| DH0-DH59             | Diseases related to eye and eye surroundings |
| DQ10-DQ15            | Congenital diseases related to eyes          |
| DS05                 | Lesion of eye and orbita                     |
| DC69                 | Cancer of eye and eye surroundings           |
| DE703                | Albinism                                      |
| KCAD                 | Removal of orbital content                   |
| KCAE                 | Surgery by anophthalmia after enucleation/evisceration of eye |
| KCDC                 | Enucleation and exenteration of the eye      |
| BCDE                 | Treatment with eye prosthesis                |
may report the variation they are experiencing at a given year instead of reporting a problem of a recurring nature. The Diagnostic and Statistical Manual of Mental Disorder (DSM-IV) criteria points out that the variation must be a recurring problem over consecutive seasons. We ask how much variation the respondent experiences across the seasons in general. The phrasing of the question is an attempt to evade this bias.

Selection bias
We believe to have contacted at least 50% of the Danish visually impaired population between the age of 18–65. DAB is a private institution that attempts to reach all eligible members. The board of DAB judges that there is no systematic bias in who chooses to be a member of their organisation. Their members are randomly distributed across demographic factors such as age, gender, income and educational level, aetiology of impairment etc.

The control group is randomly assigned on the basis of their age, gender and residential area and we therefore believe them to be a valid sample of the background population.

Sample size
A Danish survey from 1993 to 1994 found that 12% of a randomly chosen Danish population met the Kasper criteria for SAD.19 We primarily wish to investigate whether the prevalence among blind and visually impaired persons exceed 12%+5%=17%. By calculations using the SPSS sample Power V.2.0, 2004, the group of visually impaired persons must include 1260 persons or more to obtain a power of 0.95 and 1041 persons to obtain a power of 0.90. To reach adequate numbers, all 2781 eligible members of DAB are contacted.

Expecting a response rate of approximately 50% in the control group, it must include at least 2×1260=2520 matched persons.

Data analysis and statistics
Data will be analysed in SPSS V.17.0. For each group (study and control group, including subgroups with/without light perception), age (mean), gender distribution and residential distribution will be reported.

GSS will be reported by medians and IQR. Correlations between age and GSS will be tested by the Spearman correlation test for each group and gender separately. GSS differences between groups will be tested by non-parametric methods, the Mann–Whitney U test for comparing two medians and the Kruskal–Wallis test for comparing more than two medians. The medians and the corresponding p values for performed comparisons will be reported.

The prevalence of SAD and sSAD will be reported as proportions. Comparisons between groups will be tested by use of the χ² test. For each group, the proportion of respondents reporting no seasonal variation (GSS =0) will be reported and compared with other groups. In comparisons, the estimated proportions and test p values will be reported.

DISCUSSION
This study aims to investigate seasonal variation in emotional and behavioural parameters in a population of persons with severe visual impairments compared with a normally sighted control group. Any findings of differentiated patterns between subgroups of the study will support the hypothesis that light plays a role in the pathogenesis of SAD. To our knowledge, this is the first study survey to address this question.

There are various risks of bias associated with the study. The subdivision of study population respondents based on self-reported degree of visual impairment poses some uncertainty. Based on the first responses received, we see that some respondents have difficulties answering the questions or report fluctuations in the severity of their visual impairment. By the advice of our DAB contacts, we rely on the respondents’ correct report of their ability to perceive light and we will therefore solely use this parameter to differentiate between degrees of impairment. The SPAQ is based on self-report and thus holds a basis for recall bias. Our results should therefore be interpreted in terms of differentiated patterns of seasonality between groups with different visual capacities but not as estimates of the actual prevalence of SAD in our populations. The obtained prevalence estimates will also be valuable for comparisons with other groups (other nations, subgroups, etc) investigated by use of the SPAQ.

The SPAQ has been shown to lack power in separating seasonally depressed patients from non-seasonally depressed patients.22 This fact could bias the results since depression/affective disorders are a major complaint in populations with visual impairments.23 Investigations have however primarily been performed in elderly populations with visual impairments, and the findings may not necessarily extrapolate to our younger study population. Moreover, there are no indications that people with severe visual impairments should be more prone to affective disorders than people who are profoundly blind. The association between visual impairment and depression will therefore not influence the differences in the prevalence estimates for different subgroups (+/- light perception).

A risk of bias exist in the fact that people who are profoundly blind do not suffer the same dependence on lighting as less severely impaired or sighted individuals. NLP respondents may therefore experience less seasonal variation in, for example, social activities since the wintertime darkness does not practically limit their activities. To evade this problem or at least to evaluate the extent of the problem, it may be possible to perform analysis on the single questionnaire items since variation in some items cannot be explained by increased practical obstacles connected to darkness for the sighted subgroups (sleep, appetite).

An important perspective of the study is to raise awareness about the problem of SAD in the Danish visually impaired population. In this group of people, the syndrome is easily neglected, partly due to the
intuitive doubt among clinicians that seasonal changes in light can hold importance to visually impaired people or that light therapy can be effective in their treatment. From the recent increase in knowledge of the non-image-forming visual system, it seems reasonable to believe that seasonal variation in mood and behaviour may very well constitute a problem in this group. It also seems probable that the mood swings can be prevented with light therapy in visually impaired or even profoundly blind individuals. Light therapy treatment perspectives for visually impaired persons with SAD could be investigated in a randomised clinical trial with eligible respondents from our study, preferably from different impairment groups. In such a study, it will of course be necessary to perform actual clinical and paraclinical assessments of the state of vision.

In summary, it remains unclear how SAD development is related to reductions in retinal light exposure. This cross-sectional study of the prevalence of SAD in groups of people with visual impairments ranging from severe impairments to total blindness seeks to elucidate part of the question.

Contributors All authors have participated in making substantial contributions to conception and design and drafting the article or revising it critically for important intellectual content. All authors have approved the final version.

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Competing interests None.

Ethics approval The study is approved by the Danish Data Protection Agency (2010-41-4484), and personal data about the respondents are thus protected according to cf. section 50(1)(i) of the Danish Act on Processing of Personal Data. Moreover, the local ethics committee was informed of the project. The committee found that the project did not need ethical approval since it does not include any biomedical intervention. No risks are related to the project. By continued connection to DAB, we will ensure that any results of the study will be returned to the respondents and other target audience.

Provenance and peer review Not commissioned; internally peer reviewed.

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