Aim
A total of 126 11C DASB PET scans were conducted to investigate if 1) absolute levels of brain SERT binding differs between patients with SAD and healthy controls (HC), 2) if seasonal SERT fluctuations differ between groups and 3) if development of depressive symptoms is predicted by SERT changes. Seventeen SAD patients and 23 HC were assessed biannually allowing us to do the first longitudinal investigation of SAD patients.

Introduction
It is estimated that more than 15% of Copenhagen inhabitants suffer from SAD or sub-syndromal SAD [1]. Cross-sectional neuroimaging studies have demonstrated that healthy carriers of the short 5-HTTLPR polymorphism (s-carriers) have higher serotonin transporter (SERT) binding in the winter than the summer.

Methods and Results
A measure of global cerebral SERT binding (global BPND) was calculated from a volume weighted average of 17 grey matter segmented SERT regions (subcortical and cortical raphe projection areas). Group differences in absolute levels of global BPND between SAD and HC were compared summer and winter. SAD patients have significantly lower SERT levels than HC in the summer but there were no group differences in the winter.

In the longitudinal study, we used the relative change in SERT from winter to summer (relBPND) as outcome variable. We found a highly significant group effect (p=0.0002); SAD patients had higher SERT in the winter compared to summer whereas the opposite was seen in the HC (table 1 & fig.3).

In SAD patients, we tested if relBPND predicted the relative change in symptom scores from winter to summer (relSIGH-SAD) and found that a larger seasonal difference was associated with the largest difference in SAD symptoms (table 1 & fig.4).

References

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Conclusions
Healthy individuals down-regulate their SERT in winter compared to summer and SAD patients up-regulate their cerebral SERT to an extent that correlates with their SAD symptom severity. Our observations suggest a failure in SAD to regulate cerebral SERT appropriately during exposure to the environmental stress of winter, thereby contributing to the development of SAD symptoms.
Patients with seasonal affective disorder show seasonal fluctuations in their cerebral serotonin transporter binding
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Objectives: Lack of daylight is a prominent environmental stressor at high latitudes. It is estimated that more than 15% of Danish inhabitants suffer from Seasonal Affective Disorder (SAD) or sub-syndromal SAD [1]. Cross-sectional neuroimaging studies have demonstrated that in healthy individuals, striatal serotonin transporter (SERT) binding is high at winter solstice and low at summer solstice. These fluctuations are particularly evident in carriers of the short 5-HTTLPR polymorphism (S-allele carriers). The aim of the present study is to do the first longitudinal investigation of seasonal SERT fluctuations in healthy S-allele carriers and in S-allele carriers suffering from SAD.

Methods: All participants completed the Seasonal Pattern Assessment Questionnaire (SPAQ) to evaluate seasonal variations in sleep, social activity, mood, weight, appetite and energy. The score on each item was summed to obtain a Global Seasonality Score (GSS), which indexes the degree of winter depression (range: 0–24, GSS>10 indicates SAD). Subjects without any seasonality and a GSS equal to or less than 10 entered the study as healthy participants while subject with a GSS score equal to or higher than 11 were interviewed by specialized psychiatrists both in their asymptomatic and their symptomatic (winter) phase to establish the SAD diagnosis. Twenty-three (13 females) healthy S-allele carriers (mean±SD: GSS: 4.8±2 and age: 25±7 years) and 11 (six females) S-allele carrying SAD patients (mean±SD: GSS:13.7±2 and age: 26±8 years) were investigated with a dynamic [11C]DASB HRRT PET scan and a MRI brain scan both summer and winter, in randomized order. Non-displaceable binding potential (BPND) was quantified using MRTM2. Summer BPNDs were plotted as a function of winter BPND for 17 different brain regions [2]. The slope of the regression line (β) was used as a measure of individual change in global brain SERT changes across seasons. β values were compared between healthy controls and SAD patient using a Mann–Whitney unpaired t-test. A one sample paired t-test was used within groups to investigate significant seasonal SERT changes.

Results: We found a significant difference between healthy controls and SAD patients in seasonal SERT changes: median β healthy controls: 1.033, median β SAD: 0.93, U=59, p=0.01. Furthermore we observed a tendency for a winter-summer change in the SAD group (β≠1): t(10)=2.136, mean β±SD: 0.96±0.07, p=0.058 but not in the healthy control group: t(22)=1.759, mean β±SD: 1.024±0.07, p=0.092.

Conclusions: We find that SAD patients experience a significantly larger seasonal SERT fluctuation compared to their healthy counterparts. We were not able to reproduce previous findings of a similar up-regulation during winter in healthy subjects and we speculate that this is due to a careful selection of individuals completely void of season related symptoms. Our data suggests that seasonally provoked depression is linked to seasonal SERT changes.


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