



LUND UNIVERSITY

The impact of nocturnal CPAP-treatment on

Petersen, Marian

2012

[Link to publication](#)

Citation for published version (APA):

Petersen, M. (2012). *The impact of nocturnal CPAP-treatment on*. [Licentiate Thesis, Faculty of Medicine]. Lund University (Media-Tryck).

Total number of authors:

1

General rights

Unless other specific re-use rights are stated the following general rights apply:

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Read more about Creative commons licenses: <https://creativecommons.org/licenses/>

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

LUND UNIVERSITY

PO Box 117
221 00 Lund
+46 46-222 00 00

The impact of nocturnal CPAP-treatment on sexuality and closeness in patients with obstructive sleep apnoea

Thesis for doctoral degree

Marian Petersen

Department of Respiratory Medicine and Allergology

Lund University

Lund, Sweden

2012

Cover illustration: “Man and Woman” from 1960 by Anker Hoffmann (1904-1985), the City Hall Square in my hometown - Frederiksberg.

Photo by Michael Ziegler Petersen.

Copyright © Marian Petersen 2012

Department of Respiratory Medicine and Allergology

Lund University

Lund

Sweden

ISBN 1652-8220

ISSN 978-91-87189-55-5

Printed in Sweden by Media-Tryck, Lund University

Lund 2012

”Vor unge ven vil tænke det. Han kan jo købe sig et konditor-kys og se på. Jeg vil nyde. Ingen snak. Derfor står der i en gammel vise om et kys:

”es ist kaum zu sehn, es ist nur für Lippen, die genau sich verstehn,”

så nøje, at refleksionen er en næsvished og en dårskab. Den, der, når han er 20 år gammel, ikke fatter, at der er et kategorisk imperativ: nyd, er en nar, og den, der ikke griber til, bliver en christiansfelder”.

Søren Kierkegaard, ”Stadier paa Livets vei” (1845).

To Malene, Martin and
Michael

AUTHOR

Marian Petersen, RN, marian@mzp.dk

Supervisors

Bengt Midgren, MD, Ph.D., associate professor, Department of Respiratory Medicine and Allergology, Lund University, Sweden.

Søren Berg, MD, Ph.D., associate professor, Department of Otorhinolaryngology, Head and Neck surgery, Lund University, Sweden and ScanSleep, Copenhagen, Aalborg, Aarhus, Denmark.

Ellids Kristensen, MD, associate professor, Sexological Clinic, Psychiatric Centre Copenhagen, University Hospital of Copenhagen, Denmark and Department of Neurology, Psychiatry and Sensory Sciences, Faculty of Health Sciences, University of Copenhagen, Denmark.

Financial support:

Maribo Medico 2009, 2012

Spiropharma 2010

Svensk Förening för Sömnforskning och Sömnmedicin 2012

LIST OF PUBLICATIONS

- I. **Sexual function in male patients with obstructive sleep apnoea.**
Petersen M, Kristensen E, Berg S, Midgren B. Clin Respir J. 2010 Jul;4(3):186-91.
- II. **Sexual function in female patients with obstructive sleep apnea.**
Petersen M, Kristensen E, Berg S, Giraldi A, Midgren B. J Sex Med. 2011 Sep;8(9):2560-8.
- III. **Sexual function in male patients with obstructive sleep apnoea after one year of CPAP treatment.**
Petersen M, Kristensen E, Berg S, Midgren B. Clin Respir J (Epub ahead of print])
- IV. **Long-term effects of CPAP on sexuality in female OSA patients.**
Petersen M, Kristensen E, Berg S, Midgren B. (in manuscript)

TABLE OF CONTENTS

AUTHOR	4
Financial support:	4
LIST OF PUBLICATIONS	5
TABLE OF CONTENTS	6
ABBREVIATIONS	9
ABSTRACT	10
Introduction	10
Aim	11
Methods	11
Results	12
Conclusion	13
SWEDISH SUMMARY	14
Sammanfattning på svenska	14
Syfte	15
Metod	15
Resultat	16
Slutsats	16
DANISH SUMMARY	18
Sammenfatning på dansk	18
Formål	19
Metode	19
Resultater	20

Konklusion	21
INTRODUCTION	22
REVIEW OF LITERATURE	24
SEXUALITY	25
History	25
Sexuality in men and women	26
Sexual dysfunction in women	27
Sexual dysfunction in men	28
Sexual Response	29
Sexual arousal	32
SLEEP	34
Sleep stages	35
Sleep disturbances	35
Obstructive Sleep Apnoea	36
Risk factors	37
Symptoms	38
Approach	39
Obstructive sleep apnoea and sexuality	40
CPAP-treatment	40
Education	42
PRESENT STUDY	44
Aim of the thesis	44
Material and Methods	44
STATISTICAL ANALYSIS	47
SUMMARY OF RESULTS	49
Men, paper I and paper III	49
Women, paper I and paper III	51

GENERAL DISCUSSION	53
Choice of questionnaires	53
General	57
CONCLUSION AND FUTURE RESEARCH	58
ACKNOWLEDGEMENTS	59
QUESTIONNAIRES	60
REFERENCE LISTE	62

ABBREVIATIONS

AASM	American Academy of Sleep Medicine
AHI	Apnoea Hypopnoea Index
BMI	Body Mass Index
BSFI	Brief Sexual Function Inventory
CPAP	Continuous Positive Airway Pressure
CRM	Cardio Respiratory Monitoring
DSM-IV-TR	Diagnostic and Statistical Manual of Mental Disorders - IV – Text Revision
ED	Erectile Dysfunction
ESS	Epworth Sleepiness Scale
FSDS	Female Sexual Distress Scale
FSFI	Female Sexual Function Index
LiSat-11	Life Satisfaction 11
MFSD	Manifest Female Sexual Dysfunction
NREM	Non Rapid Eye Movement
OSA	Obstructive Sleep Apnoea
PE	Premature Ejaculation
PDE5	Phosphodiesterase type 5 inhibitor
PSG	Polysomnography
REM	Rapid Eye Movement
SSRIs	Selective Serotonin Reuptake Inhibitors

ABSTRACT

Introduction

Sleep has a major impact on our wellbeing and how we perform. If we have interrupted sleep for a couple of nights we will experience daytime tiredness and if the interruption lasts over a longer period it may influence our mood, our relationships with other people and our general health.

OSA has an estimated prevalence of 2 % in women and 4 % in male and is characterized by repetitive complete (apnoea) or partial (hypopnoea) cessation of breathing. The consequences are often dramatic. After an apnoea, which in serious cases may last for more than a minute, breathing starts with a loud gasp often followed by loud snoring. Struggling for breath the patient may exhibit violent jerks of the body and extremities, alarming and often terrifying their bed-partner.

When I worked at Respiratory Center East I wondered how the patients managed sexuality and closeness when suffering from OSA and in particular how the Continuous Positive Airways Pressure (CPAP) treatment affected their sexuality and closeness. Maybe due to my own prediction expecting elderly to “prioritize” treatment efficacy to vanity, I thought that it would be easier for elderly patients to accept CPAP than it would for younger patients. Elderly patients might have been in a relationship for a longer time and because of that be more close to the partner. However, when asking about difficulties regarding sexuality and relationship to their partner the answers were not always as I expected. I have met a 26 year old man who did not use the device every night - but always used it when he slept with his girlfriend. She refused to sleep beside him if he did not use the CPAP device, to avoid loud snoring and apnoeas. Nor did another male patient 72 year old use his CPAP device every night. He always used it when he slept alone but never when he slept with his girlfriend. Actually she did not know that he had OSA and was treated with CPAP. He found it too embarrassing to tell her.

A review of the literature showed there was little published information concerning the impact of CPAP treatment on sexuality, why it was difficult to advise the patients on this matter and how to predict whether closeness to one's partner would be reduced or improved when treated with CPAP. Furthermore, in order to guide and inform a patient as to how CPAP treatment may affect sexuality

you have to know about sexual function and dysfunction as well as the difference between women and men. Therefore, in order to clarify the relationship between OSA, CPAP-treatment and sexuality this thesis was made.

Aim

The overall aim of this thesis was to study the impact of nocturnal CPAP treatment on sexuality and closeness in patients with obstructive sleep apnoea.

The specific aims were:

Paper I: To investigate general and functional aspects of sexuality in male patients with a confirmed diagnosis of Obstructive Sleep Apnoea (OSA) and compare the results to normative data. Paper II: To investigate sexual difficulties and sexual distress in female patients with obstructive sleep apnoea and to determine which factors are of importance to their sexual function. Paper III: To investigate what impact one year of effective nocturnal CPAP treatment has on general and functional aspects of sexuality in male patients with a confirmed diagnosis of Obstructive Sleep Apnoea (OSA). Paper IV: To describe the impact of CPAP treatment on sexual difficulties and sexual distress in female patients with OSA after one year on treatment.

Methods

Patients with a diagnosis of OSA were consecutively recruited from the sleep clinic ScanSleep from October 2005 to January 2008. After recruitment, 308 men and 92 women were included and after one year 150 men and 44 women remained in the study. The study comprised only patients ≥ 18 years old, able to read and write Danish and with a diagnosis of OSA requiring treatment with CPAP.

Data was collected by self-reported questionnaires. The Epworth Sleepiness Scale (ESS) assesses the likelihood of the patient dozing off or falling asleep in eight daily situations. The Life Satisfaction 11 (LiSat-11) concerns general satisfaction with life. After personal communication with the author of the questionnaire, asking which questions could be used to investigate closeness, we used four questions: Life as a Whole and three domains of closeness (Sexual Life, Partner Relationship, Family Life). Furthermore we asked for socio-demographic data on age, body mass index (BMI), marital status, education and current use of medication.

The specific sexual questionnaire for men was the Brief Sexual Function Inventory (BSFI) in which the first 10 items cover functional aspects of male sexual function during the past 30 days. The specific sexual questionnaires for women were the Female Sexual Function Index (FSFI) and the Female Sexual Distress Scale (FSDS). FSFI measures female sexual function in women with a sexual partner. FSDS measures sexual-related distress in women. Manifest Female Sexual Dysfunction (MFSD) is present when the respondent has both sexual difficulty and sexual distress.

From Sweden, Fugl-Meyer LiSat-11 data were collected by questionnaires and face-to-face interviews, and participants were drawn from the Swedish Central Population Register (14) and from Norway. For BSFI participants were recruited by using public address lists and sending questionnaires (16). The women used as controls were participants from a cross-sectional national survey of Danish women's sexual life. A total of 1,996 Danish women were identified from the central health registry. From the respondents, we selected 240 women age-matched to the OSA group – three from the control group for each OSA patient and including their raw data in our analyses.

Results

Male. Paper I. We found that both general (LiSat-11) and functional (BSFI) aspects of sexuality were worse in patients with (untreated) OSA when compared with normative data. Both aspects were dependent on age, obesity, social factors and concomitant medication but not on the severity of OSA. Paper III. Satisfaction with Sexual Life (Li-Sat 11) and both general and functional aspects of sexuality (BSFI) were significantly improved after 1 year of CPAP treatment. Daytime sleepiness (ESS) decreased significantly after 1 year of CPAP treatment.

Female. Paper II. Females with untreated OSA were at a higher risk for having sexual difficulties, sexual distress and sexual dysfunction compared to the population sample. Severity of sleep apnoea was, however, not related to any of these indices, but consumption of psychopharmaca was. Regarding life satisfaction (Lisat-11), female patients with obstructive sleep apnoea scored lower than women in the population sample. Paper IV. Manifest Female Sexual Dysfunction was significantly improved after one year of CPAP treatment, but no significant changes in isolated sexual difficulties or sexual distress were found. Daytime sleepiness (ESS) decreased significantly after 1 year of CPAP treatment.

Conclusion

Daytime sleepiness decreased significantly in both male and female, indicating a positive effect of CPAP treatment. Sexuality improved both in general and specific aspects in male patients and female patients had a decrease in sexual dysfunction. We consider it important to be aware of the gender when assessing a patient's sexual function. Furthermore regarding women, you have to keep in mind you have to divide sexual function into difficulties and distress and that only when both are present is sexual dysfunction considered. It is important to underline that all patients in our studies had identical diagnostic procedures performed and received the same instructions, follow-up and treatment contacts. The strength of our study is that it was sufficiently long to allow for adaptation of CPAP treatment which often takes at least a couple of months.

Many patients may be reluctant to use a treatment involving the use of a mask, a tube and machine every night for many years to come. However, one of our main findings is that CPAP treatment per se does not negatively affect family life or partner relationship. We consider this important information when initiating CPAP treatment.

SWEDISH SUMMARY

Sammanfattning på svenska

Sömnen har en stor inverkan på vårt välbefinnande och hur vi arbetar. Om vi har splittrad sömn några nätter kommer vi att uppleva trötthet under dagtid, och om problemet fortsätter under en längre tid kan det påverka humör, relationer med andra människor och hälsa i allmänhet.

Obstruktiv sömnapné (OSA) har en uppskattad prevalens på 2 % hos kvinnor och 4 % hos män och kännetecknas av upprepade partiella eller totala stopp för andningen (hypopné respektive apné). Händelseförloppet är ofta dramatiskt. Efter en apné, som i svåra fall kan pågå i mer än en minut, börjar andningen med en hög flämtning ofta följt av högljudda snarkningar. Patienter som kämpar för att få luft kan uppvisa våldsamma ryckningar i kroppen och extremiteterna, vilket kan vara skrämmande för sängpartnern.

När jag arbetade på RespirationsCenter Øst i Köpenhamn, undrade jag vad som hände med patienternas sexualitet och intimitet medan de kämpade med OSA, och särskilt hur behandling med CPAP (Continuous Positive Airway Pressure) påverkat deras sexualitet och intimitet. Kanske på grund av mina egna förväntningar att äldre människor prioriterar effekten av en behandling snarare än fåfänga, trodde jag det skulle vara lättare för äldre patienter än för unga för att acceptera CPAP behandling. Dock var svaren inte alltid som jag förväntat, när jag frågade patienten om sexualitet och relationen med sin partner. Jag har träffat en 26-årig man som inte använde CPAP varje natt - men alltid när han sov med sin flickvän. För att slippa hans högljudda snarkningar och andningsuppehåll vägrade hon att sova bredvid honom, om han inte använde CPAP. En annan manlig patient, på 72 år, använde inte CPAP varje kväll. Alltid när han sov ensam, men aldrig när han sov med sin partner. Egentligen visste hon inte att han hade OSA och behandlades med CPAP. Han fann det för pinsamt att berätta för henne.

Jag upplevde en brist på information i litteraturen om effekterna av CPAP på sexualitet, vilket gjorde det svårt att ge råd och att vägleda patienter och att förutsäga om intimitet och närhet till en partner blev bättre eller sämre, när de behandlades med CPAP. För att vägleda och informera patienten om hur CPAP påverkar sexualiteten behöver du kunskaper om sexuell funktion och dysfunktion

och skillnaden mellan kvinnor och män. Meningen med denna avhandling är att klargöra förhållandet mellan OSA, CPAP-behandling och sexualitet.

Syfte

Det övergripande syftet med denna avhandling är att studera den sexuella funktionen hos patienter med OSA – före CPAP och efter en period av effektiv CPAP-behandling.

De specifika målen är följande:

Studie I: Att undersöka de allmänna och funktionella aspekterna av sexualitet hos manliga patienter med diagnostiserad obstruktiv sömnapné (OSA) och jämföra resultaten med kontrollgrupper. Studie II: Att undersöka sexuell problem och sexuella bekymmer hos kvinnliga patienter med obstruktiv sömnapné och att avgöra vilka faktorer som är viktiga för deras sexuella funktion. Studie III: Att undersöka konsekvenserna av ett års effektiv nattlig CPAP-behandling på allmänna och funktionella aspekter av sexualitet hos manliga patienter. Studie IV: Att beskriva effekten av CPAP-behandling på sexuella problem och sexuella bekymmer hos kvinnliga patienter med OSA efter ett års behandling.

Metod

Patienter med OSA rekryterades från ScanSleep från oktober 2005 till januari 2008. Vi rekryterade konsekutivt 308 män och 92 kvinnor till studiestart och efter ett år återstod 150 män och 44 kvinnor i undersökningen. I studien ingick endast patienter ≥ 18 år gamla, som kunde läsa och skriva danska och med diagnosen OSA som kräver behandling med CPAP.

Data samlades in med hjälp av självrapporterade frågeformulär. Epworth Sleepiness Scale (ESS) bedömer sannolikheten för att man slumrar eller somnar i åtta vardagliga situationer. Life Satisfaction 11 (LiSat-11) mäter den totala tillfredsställelsen med livet: livet som helhet och de tre domänerna av närhet (sexualliv, relation till partner och familjeliv). Vidare frågade vi om socio-demografiska uppgifter; ålder, body mass index (BMI), civilstånd, utbildning och användning av läkemedel.

Frågeformulär för sexualitet specifikt för män var Brief Sexual Funktion Inventory (BSFI), som täcker in funktionella aspekter och allmän sexuell tillfredsställelse under de senaste 30 dagarna. Frågeformulär för sexualitet specifikt för kvinnor var

Female Sexual Function Index (FSFI) och Female Sexual Distress Scale (FSDS). FSFI frågar om sexuell funktion hos kvinnor med partner. FSDS frågar om sexuella bekymmer. Från svaren på FSFI och FSDS kan man beräkna om kvinnan har sexuell dysfunktion.

Den kvinnliga kontrollgruppen för FSFI och FSDS var deltagare från en dansk populationsbaserad longitudinell undersökning av kvinnors sexuella liv. Den manliga jämförelsegruppen för BSFI var från en norsk studie, där deltagarna rekryterades från det centrala befolkningsregistret. För både kvinnor och män för LiSat-11 var jämförelsegruppen hämtad ur en studie från Sverige och rekryterad från det centrala befolkningsregistret.

Resultat

Män. Studie I. Både allmänna (LiSat-11) och funktionella (BSFI) aspekter av sexualitet var sämre hos patienter med (obehandlad) OSA jämfört med kontrollgruppen. Båda aspekterna var beroende på ålder, fetma, sociala faktorer och samtidig medicinering, men inte svårighetsgraden av OSA. Studie III. Tillfredsställelse med sexualliv (LiSat-11) och både allmänna och funktionella aspekter av sexualitet (BSFI) var signifikant förbättrade efter 1 års CPAP-behandling. Dagtröttheten minskade signifikant efter 1 års CPAP-behandling.

Kvinnor. Studie II. Kvinnor med obstruktiv sömnapné har en högre risk att få sexuella problem, sexuell oro och sexuell dysfunktion jämfört med kontrollgruppen. Svårighetsgraden av OSA påverkade inte utfallet av de studerade variablerna, men bruk av mediciner för psykiska sjukdomar hade ett stort inflytande. Avseende tillfredsställelse med livet som helhet (Lisat-11) hade kvinnliga patienter med obstruktiv sömnapné sämre värden än kontrollgruppen. Studie IV. Sexuell dysfunktion var signifikant förbättrad efter ett års behandling med CPAP. Det fanns inga signifikanta förändringar avseende sexuella problem och sexuella bekymmer. Dagtröttheten minskade signifikant efter ett år.

Slutsats

Dagtröttheten minskade signifikant bland både kvinnor och män, vilket bekräftar en positiv effekt av CPAP-behandling. Sexualiteten förbättrades både generellt och specifikt bland de manliga patienterna, i motsats till resultaten för de kvinnliga patienterna. Vi anser det viktigt att vara uppmärksam på kön, när det handlar om att prata med en patient om hans / hennes sexuella funktion. Dessutom, hos

kvinnor, att komma ihåg att man måste dela upp den sexuella funktionen i sexuella problem och sexuella bekymmer. Endast när båda föreligger kan man prata om sexuell dysfunktion. Det är viktigt att betona att alla patienter i vår studie oavsett kön genomgick identiska procedurer för diagnostik, fick samma instruktioner och hade samma uppföljning av den fortsatta behandlingen. Styrkan i vår studie är att studien höll på tillräckligt länge för att möjliggöra justering av CPAP-behandlingen, som ofta tar minst några månader.

Många patienter kan vara ovilliga att använda en behandling som innebär användning av en mask, en slang och en maskin varje kväll. Ett av våra viktigaste resultat är dock att CPAP behandlingen i sig inte påverkar familjeliv eller förhållande negativt. Vi anser att denna information är viktig när man startar CPAP-behandling.

DANISH SUMMARY

Sammenfatning på dansk

Søvn har en stor indflydelse på vores velbefindende, og hvordan vi fungerer. Hvis vi har afbrudt søvn et par nætter, vil vi opleve træthed i dagtimerne, og hvis afbrydelsen varer over en længere periode, kan det have indflydelse på humøret, forholdet til andre mennesker og sundhed i almindelighed.

Obstruktiv Søvn Apnø (OSA) har en anslået forekomst på 2 % hos kvinder og 4 % hos mænd og er kendetegnet ved gentagne hele eller delvise ophør af vejrtrækningen (apnø / hypopnø). Scenariet er ofte dramatisk for tilskueren. Efter en apnø, som i alvorlige tilfælde kan vare i mere end et minut, begynder vejrtrækningen med et højt gisp ofte efterfulgt af højlydt snorken. Patienten, der kæmper for at få luft, kan udvise voldsomme ryk i kroppen og ekstremiteter, hvilket kan være skræmmende for sengepartneren.

Da jeg arbejdede på Respirationcenter Øst, Rigshospitalet i København spekulerede jeg på, hvordan patienterne klarede seksualiteten og intimiteten, samtidigt med de kæmpede med OSA, og navnlig hvordan CPAP behandlingen (Continuous Positive Airway Pressure) påvirkede deres seksualitet og intimitet. Måske på grund af min egen forventning om, at ældre vil prioritere effekt af en behandling fremfor forfængelighed, tænkte jeg, at det ville være lettere for ældre patienter end for yngre at acceptere CPAP behandlingen. Dog var svarene ikke altid, som jeg forventede, når jeg spurgte den enkelte patient til brugen af CPAP udstyret. Jeg har mødt en 26-årig mand, der ikke brugte CPAP apparatet hver nat - men altid, når han sov med sin kæreste. For at undgå at blive holdt vågen af høj snorken og apnø nægtede hun at sove ved siden af ham, hvis han ikke brugte CPAP apparatet. En anden mandlig patient på 72 år brugte heller ikke sit CPAP apparat hver nat. Altid når han sov alene, men aldrig når han sov med sin kæreste. Faktisk vidste hun ikke, at han havde OSA og blev behandlet med CPAP. Han fandt det for pinligt at fortælle hende.

Jeg oplevede en mangel på oplysninger i litteraturen om effekten af CPAP-behandling på seksualitet, hvilke gjorde det svært at rådgive og vejlede

patienterne, samt at forudsige om intimitet og nærhed til ens partner blev reduceret eller forbedret, når de blev behandlet med CPAP. For kunne vejlede og informere en patient, hvorvidt CPAP-behandling påvirker seksualiteten, behøver du viden om seksuel funktion og dysfunktion samt forskellen mellem kvinder og mænd. Denne afhandling blev skrevet med henblik på at afklare forholdet mellem OSA, CPAP-behandling og seksualitet.

Formål

Det overordnede formål med denne afhandling er at studere den seksuelle funktion hos patienter med OSA - før CPAP behandlingen og efter en periode med effektiv CPAP behandling.

De specifikke mål er:

Studie I: At undersøge de generelle og funktionelle aspekter af seksualitet hos mandlige patienter med en bekræftet OSA-diagnose og sammenligne resultaterne med en kontrol gruppe. Studie II: At undersøge seksuelle problemer og seksuelle bekymringer hos kvindelige patienter med OSA, samt at afgøre hvilke faktorer der er af betydning for deres seksuelle funktion. Studie III: At undersøge hvilke konsekvenser et års effektiv natlig CPAP behandling har for generelle og funktionelle aspekter af seksualiteten hos mandlige patienter med OSA. Studie IV: At beskrive effekten af CPAP behandling på seksuelle problemer og seksuelle bekymringer hos kvindelige patienter med OSA efter et års behandling.

Metode

Patienter med OSA blev konsekutivt rekrutterede i ScanSleep fra oktober 2005 til januar 2008. Efter endt rekruttering var 308 mænd og 92 kvinder inkluderede og efter et år var der 150 mænd og 44 kvinder tilbage i undersøgelsen. Undersøgelsen omfattede kun patienter ≥ 18 år gamle, i stand til at læse og skrive dansk og med OSA, som krævede behandling med CPAP.

Data blev indsamlet ved hjælp af selvrapporterede spørgeskemaer. Epworth Sleepiness Scale (ESS) vurderer sandsynligheden for, at man døser hen eller falder i søvn i otte daglige situationer. Life Satisfaction 11 (LiSat-11) måler generel tilfredshed med livet: liv som helhed og tre domæner af nærhed (seksualliv, relation til partner og familieliv). Desuden spurgte vi om socio-demografiske data

vedrørende alder, body mass index (BMI), ægteskabelig status, uddannelse og brug af medicin.

Spørgeskema vedrørende specifik seksualitet for mænd var Brief Sexual Function Inventory (BSFI), hvori der spørges til den seksuelle funktion samt den samlede seksuelle tilfredshed i løbet af de seneste 30 dage. Spørgeskemaer vedrørende seksualitet for kvinder var Female Sexual Function Index (FSFI) og Female Sexual Distress Scale (FSDS). FSFI spørger til seksuel funktion hos kvinder med en seksuel partner. FSDS spørger til bekymring for seksualiteten. Ud fra svarene i FSFI og FSDS kan man udregne, hvorvidt kvinden har seksuel dysfunktion.

Den kvindelige kontrolgruppe for FSFI og FSDS var deltagere fra en dansk national tværsnitsundersøgelse af kvinders seksualliv. Den mandlige kontrolgruppe for BSFI var fra Norge, hvor deltagerene blev rekrutteret fra det norske central personregister. For både kvinder og mænd var kontrolgruppen for LiSat-11 fra Sverige rekrutteret fra det svenske centrale personregister.

Resultater

Mænd. Studie I. Både tilfredshed med livet (LiSat-11) og specifikke aspekter (BSFI) af seksualitet var værre hos patienter med (ubehandlet) OSA, når der blev sammenlignet med kontrolgruppen. Begge tilfælde var afhængige af alder, overvægt, sociale faktorer og samtidig medicin, men ikke af sværhedsgraden af OSA. *Studie III.* Tilfredsheden med seksuallivet (LiSat-11) og både generelle og funktionelle aspekter af seksualitet (BSFI) var signifikant forbedret efter 1 års CPAP behandling. Dagtræthed faldt signifikant efter 1 års CPAP behandling.

Kvinder. Studie II. Kvinder med (ubehandlet) obstruktiv søvnapnø havde en højere risiko for at have seksuelle problemer, seksuelle bekymringer samt seksuel dysfunktion i forhold til kontrolgruppen. Sværhedsgraden af OSA havde ikke relation til den kvindelige seksualitet, hvorimod brug af medicin mod psykiske lidelser havde stor indflydelse. I forhold til tilfredshed med livet som helhed (LiSat-11) scorede kvindelige patienter med obstruktiv søvnapnø lavere end kontrolgruppen. *Studie IV.* Seksuel dysfunktion var væsentligt bedret efter et års behandling med CPAP. Der var ingen ændringer i forhold til seksuelle problemer og seksuel bekymring. Dagtræthed faldt betydeligt efter et år.

Konklusion

Dagrætheden faldt betydeligt hos både kvinder og mænd, hvilket indikerer en positiv effekt af CPAP behandlingen. Seksualiteten blev forbedret både generelt og specifikt hos de mandlige patienter, hvilket er i modsætning til resultatet hos kvindelige patienter. Vi anser det for vigtigt at være opmærksom på kønnet, når man som behandler taler med en patient om hendes / hans seksuelle funktion. Desuden at huske på at man hos kvinder bliver nødt til at opdele den seksuelle funktion i seksuelle problemer og seksuelle bekymringer, og at man, kun når begge dele er tilstede, kan tale om seksuel dysfunktion. Det er vigtigt at understrege, at alle patienter i vore studier havde identisk udførte procedurer i forhold til diagnostik, havde modtaget de samme instruktioner samt havde haft ens opfølgning og behandlingskontakt. Styrken i vore undersøgelser er, at undersøgelsen foregik over tilstrækkelig lang tid til at tillade adækvat tilpasning af CPAP behandling, som ofte tager mindst et par måneder.

Mange patienter kan være tilbageholdende med at bruge en behandling, der involverer brugen af en maske, en slange og en maskine hver nat. Et af vores vigtigste resultater er derfor, at CPAP behandling i sig selv ikke påvirker familielivet eller parforholdet negativt. Vi anser denne oplysning vigtig ved indledning af CPAP behandling.

INTRODUCTION

If asked, we all know how we have been sleeping. Maybe we do not know why we slept well or poorly, but everyone can answer the question. Sleep has a major impact on our wellbeing and how we perform. If we have interrupted sleep for a couple of nights we will experience daytime sleepiness and if the interruption lasts over a longer period, it may influence our mood, our relationships with other people and our general health.

For eight years I worked in the Respiratory Center East in Copenhagen meeting patients who had different types of respiratory sleep disorders. Many of the patients suffered from Obstructive Sleep Apnea (OSA), a condition occurring during sleep, but due to the sleep disruption it causes, very much affecting patients when they are awake. OSA has an estimated prevalence of 2 % in women and 4 % in men and is characterized by repetitive complete (apnoea) or partial (hypopnoea) cessation of breathing. The consequences are often dramatic. After an apnea, which in serious cases may last for more than a minute, breathing starts with a loud gasp often followed by loud snoring. Struggling for breath the patient may exhibit violent jerks of the body and extremities, alarming and often terrifying their bed-partner. As these episodes occur repeatedly, these nocturnal occurrences are often the reason why the bed partner demands the person with OSA be examined and treated.

When I worked at Respiratory Center East I wondered how the patients managed sexuality and closeness when suffering from OSA and in particular how the Continuous Positive Airways Pressure (CPAP) treatment affected their sexuality and closeness. Maybe due to my own prediction expecting elderly to “prioritize” treatment efficacy to vanity, I thought that it would be easier for elderly patients to accept CPAP, than it would for younger patients. Elderly patients might have been in a relationship for a longer time and because of that be more close to the partner. However, when asking about difficulties regarding sexuality and relationship to their partner the answers were not always as I expected. I have met a 26 year old man who did not use the device every night - but always used it when he slept with his girlfriend. She refused to sleep beside him if he did not use the CPAP device to avoid loud snoring and apnoeas. Nor did another 72 year old male patient use his CPAP device every night. Always when he slept alone, but never when he slept with his girlfriend. Actually she did not know that he had OSA and was treated

with CPAP. He found it too embarrassing to tell her. Both patients found the use of a mask very 'unsexy', but had realized that daytime sleepiness decreased when using the CPAP.

A review of the literature showed there was little published information concerning the impact of CPAP treatment on sexuality, why it was difficult to advise the patients in this matter and to predict whether closeness to one's partner would be reduced or improved, when treated with CPAP. Furthermore, in order to guide and inform a patient as to how CPAP treatment may affect sexuality you have to know about sexual function and dysfunction, as well as the difference between women and men. Therefore, in order to clarify the relationship between OSA, CPAP-treatment and sexuality this thesis was made. In the following sections I will describe the areas that I have investigated in my study.

REVIEW OF LITERATURE

When I initiated my paper I found a paucity of published articles. Using PubMed for review of literature and using filters “Humans” and “English articles only”, the result showed a paucity of articles regarding OSA and sexuality. Repeating the reviewing after five years and using the same filters “Humans” and “English” articles only, shows that research regarding OSA and sexuality is increasing, but still the number of articles is very small compared to other disorders that one commonly links to OSA; “cardiovascular disorder and sexuality” and “diabetes and sexuality”. Only metabolic syndrome shares almost the same small number of articles regarding sexuality (table 1).

Table 1 PubMed review of literature regarding sexuality at study start and after five years.

Keyword	Hit 2007.07.31	Hit 2012.09.22	Increase in %
OSA AND sexuality	7	12	71
OSA AND sexuality AND male	7	11	57
OSA AND sexuality AND female	6	8	33
OSA AND sexual function	5	9	80
OSA AND sexual function AND male	5	8	60
OSA AND sexual function AND female	2	3	50
OSA AND sexual dysfunction	5	11	120
OSA AND sexual dysfunction AND male	5	10	100
OSA AND sexual dysfunction AND female	1	2	100
Metabolic syndrome AND sexuality	23	46	100
Metabolic syndrome AND sexuality AND male	13	25	92
Metabolic syndrome AND sexuality AND female	14	25	79
Cardiovascular disorder AND sexuality	786	995	27
Cardiovascular disorder AND sexuality AND male	583	723	24
Cardiovascular disorder AND sexuality AND female	460	600	30
Diabetes AND sexuality	263	386	47
Diabetes AND sexuality AND male	199	277	39
Diabetes AND sexuality AND female	157	223	42

SEXUALITY

History

Sexuality has during all periods in history been firmly a part of human life as numerous writings from antiquity to the present day testify. In spite of this, the noun “sexuality” first appeared in the beginning of 1800 in the field of botanics. Shortly after it transferred to the field of human sexuality, but initially the term was reserved for the various aspects of reproduction and not for sexual desire. In Europe in the 19th century sexual subjects were considered taboo. However many scientists brought up new ideas about sexuality during this period and in the first part of 20th century sexuality began to contain the term of sexology as we know it today.

In 1908 the first journal of sexology was established in Berlin by Magnus Hirschfeld, though the journal was only published for one year. The journal was re-started in 1914 by Iwan Bloch and Albert Eulenburg. In 1919 Magnus Hirschfeld established the Institute of Sexology, the first such institute in Europe – located in the center of Berlin. The Institute provided public information and education, as well as treatment of patients and scientific research. Magnus Hirschfeld organized the first “International Congress of Sexology” in 1921 and thereby initiated an international cooperation of sexologists.

World War II put a stop to the development and research in sexology. In the postwar period, Alfred Kinsey from USA may be considered as the pioneer in the quantitative and epidemiologic study of human sexuality. Especially the “Kinsey Report” from 1948 contributed to the knowledge of sexual behavior, not only in the USA, but in the Western world as well.

In Denmark the Psychiatric Department, Rigshospital in Copenhagen, started to offer treatment to patients with sexual problems in mid-1970. In 1980 the parliament decided to establish a Sexological Clinic at the Rigshospital and in 1986 the Sexological Clinic was ready. Nowadays the Sexological Clinic has a range of functions; treatment of patients with sexological problems; anonymous telephone consulting; education and research.

Sexuality in men and women

The expression of sexuality is individual, changes through life and there are interpersonal differences as well as differences between women and men. Unawareness of these differences may cause misinterpretation of information given by the patient. The differences can be quite large i.e. men can accurately assess their own genital engorgement which encourages further arousal, whereas women often are more complex and need to have mental calm, intimacy and gentle stimulus to get sexually aroused. When asking a patient about her/his sexuality you have to question their sexual function and for women you have to question sexual distress as well, because the two items are not necessarily present at the same time. However from research point of view there is no distinct measure of sexual distress in men.

Many factors have an impact on the sexuality (table 2), such as interpersonal difficulties, low self-image, absence of needed sexual stimuli or sexual skills in either partner.

Table 2 Overview of medical and psychosocial effects of disease on sexual function. (Basson and Schultz, Lancet 2007, 369:409-24)

<p>Medical factors resulting from disease, treatment, or both</p> <ul style="list-style-type: none">• Fatigue, pain, incontinence, or changed anatomy of sexual organs• Reduced mobility which limits ability to caress, stimulate self or partner, or engage in intercourse• Changed physical sensations, such as itching, irritation, insensitivity, or hypersensitivity• Interruption of sexual response, infertility, dyspareunia, or painful ejaculation or orgasm• Angina or dyspnea from sexual stimulation <p>Psychological response to illness or sexual dysfunction</p> <ul style="list-style-type: none">• Fear that sex could be dangerous, and provoke myocardial infarction or cerebral vascular accident• Fear of infection or conviction that illness was caused by sexual activity (e.g. cancer as punishment)• Preoccupation with illness or loss of control and independence• Disrupted sexual self-image or feeling failure as a sexual partner or potential parent• Anxiety, depression, anger, shame, guilt, stress, or emotional lability.• Avoidance behavior, fearing pain or rejection due to disfigurement or stomas• Repeatedly remembering traumatic medical procedures to sexual parts <p>Personal psychological factors</p> <ul style="list-style-type: none">• Limited coping mechanisms or negative attitude• History of limited or unrewarding sexual experiences• Past abuse (sexual, physical, or emotional) <p>Relationship and social factors</p> <ul style="list-style-type: none">• Lack of intimacy, trust, or freedom from abuse• Difficulties with communication, power regulation, or role change• Partner's negative reaction to illness• Partner's sexual dysfunction• Inability to meet a partner or lack of information about sexual rehabilitation• Social obstruction by third parties (e.g. at hospital or nursing home)• Cultural non-acceptance of sexuality when ill or old

Considering all factors affecting sexual life one may wonder when sexual life is 100 % at its top. Early medical science considered that sexual dysfunction had either psychological or physiological origins. Nowadays it is well known that in most cases the two are inseparably combined and sexuality is an interaction between partners and must be seen from a bio psychosocial perspective (1).

Sexual dysfunction in women

Women's sexual dysfunction may include reduced interest for sexual engagement, difficulties with becoming subjectively aroused and/or genitally aroused and difficulties in triggering desire during sexual engagement. Anorgasmia is defined when arousal is present but there is an absence of orgasm. Dyspareunia is defined as when pain occurs with intercourse or any attempts at vaginal penetration.

The prevalence of sexual dysfunction in women is highly variable depending on which study you read and how sexual dysfunction is defined. According to the DSM-IV-TR (Diagnostic and Statistical Manual of Mental Disorders-IV-Text Revision) sexual difficulty has to be recurrent and persistent and cause marked distress or interpersonal difficulty to be considered as sexual dysfunction (2). Thus, reported sexual problems or sexual difficulties may not always be equal to sexual dysfunction. Christensen *et al.* (2) found in a study among 2295 Danish women, age 16 – 95 years who were sexually active, the prevalence for various types of sexual dysfunction (frequent and perceived as a problem) and their respective sexual difficulty (not considered to be problematic): Lubrication insufficiency in 7% / 50%, Anorgasmia in 6% / 63% and Dyspareunia in 3% / 25%. In a global study Laumann *et al.* (3) investigated the prevalence of women's sexual problems, using a definition of sexual problem as a periodic or frequent sexual problem during a period of a year, they found: Lubrication difficulties 16% - 38%, Anorgasmia 18% - 41% and Dyspareunia 9% - 32%. However, they did not ask about sexual distress. The prevalence in the two above mentioned studies show how wide the differences may be, but leaves no doubt about the severity regarding that sexual function in women is an area that should continue to be explored.

The treatment of sexual dysfunction in women is of course dependent on the specific problem. Regarding low desire and low arousal, cognitive behavior techniques based on the theory that thoughts, feelings, and behaviors interact and mutually influence one another and newer cognitive behavior techniques, integrating mindfulness meditation, has been shown to benefit up to 74% of couples. Treatment of dyspareunia includes chronic pain medication along with sexual and psychological methods (4).

Sexual dysfunction in men

Erectile dysfunction (ED) (a man's consistent or recurrent inability to attain and/or maintain penile erection sufficient for sexual activity) and premature ejaculation (PE) (ejaculation before vaginal penetration or < 1-2 min afterwards) are the two most common sexual dysfunctions in the male (5). When clarifying the reasons for ED and/or PE you need to ask about the severity, onset, and duration of the problem as well as the presence of concomitant medical or psychosocial factors. Is the presenting complaint the primary or major sexual problem or is some other aspect of the sexual response cycle involved (figure 3)?

Choosing the two above mentioned studies (2;3) and DSM-IV-TR's definition of sexual dysfunction and sexual difficulties, the prevalence in males of sexual dysfunction and related sexual difficulty are: Erectile difficulties 5% / 35% and premature ejaculation 7% / 54% (2). Laumann *et al.* (3) found: Erectile difficulties 13% - 28% and premature ejaculation 12% - 31%.

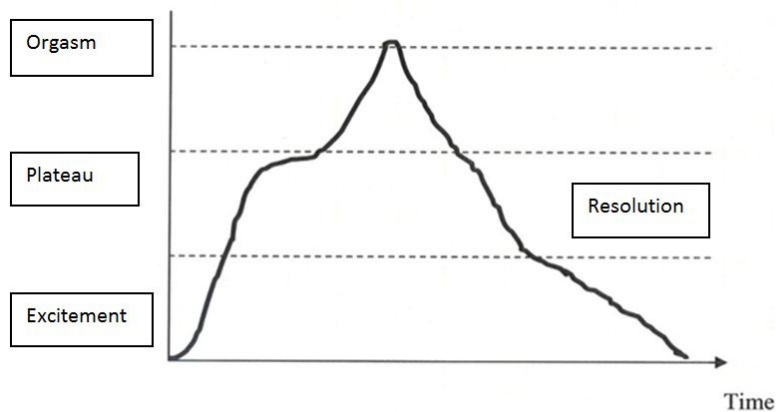
Prevalence of ED increases with age but several risk factors are involved such as lack of exercise, obesity, smoking, hypercholesterolemia, and metabolic syndrome. Modifying these risk factors may reduce ED. Medical treatment of ED utilizes the phosphodiesterase type 5 inhibitors (PDE5) such as Sildenafil, Vardenafil, and Tadalafil. Furthermore psychological treatment such as: psychodynamic interpretations regarding anxiety, sensate focus, couples therapy, sex education, communication and sexual skills training, and masturbation exercises, may have a positive effect on ED.

The prevalence of PE is not affected by age. Risk factors for PE are unknown, but linked to self-confidence, relationship with the partner, mental distress, anxiety, embarrassment, and depression. Medical treatment such as selective serotonin reuptake inhibitors (SSRIs) e.g. Paroxetine, Sertraline, and Fluoxetine may be useful treatments for PE. Beside medical treatment, self-control techniques to delay ejaculation may be a helpful way to control ejaculation (4). Furthermore psychosexual therapy helping the patient to recover his self-confidence by reducing performance anxiety, solving relational problems, increasing communication between partners, and modifying rigid sexual repertoires, may help couples remove barriers to intimacy.

Sexual Response

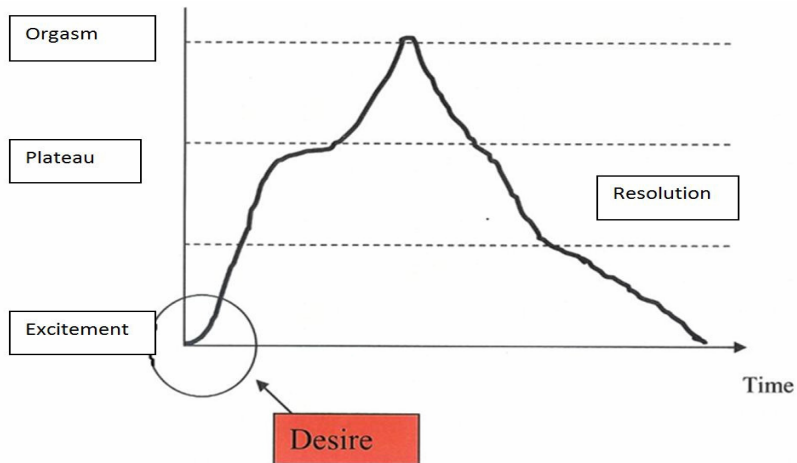
There are different reasons for wanting to have sex with a partner. Sexual desire is one reason but also important may be the enhancement of emotional closeness, bonding, commitment, a desire to increase a sense of attractiveness and attraction to a partner or a desire to share physical sexual pleasure. When talking about sexual response several models have being discussed through time. In 1966 Masters and Johnson characterized the sexual response cycle consisting of four phases: sexual arousal/excitement, plateau, orgasm, and resolution (figure 1). Each phase is associated with genital changes, and focuses almost exclusively on bodily responses to sexual stimulation, with almost no attention being given to the cognitive or subjective aspects of sexual response.

Figure 1 Linear model of human sexual response. Masters WH, Johnson VE, Human. Human Sexual Response, 1966.



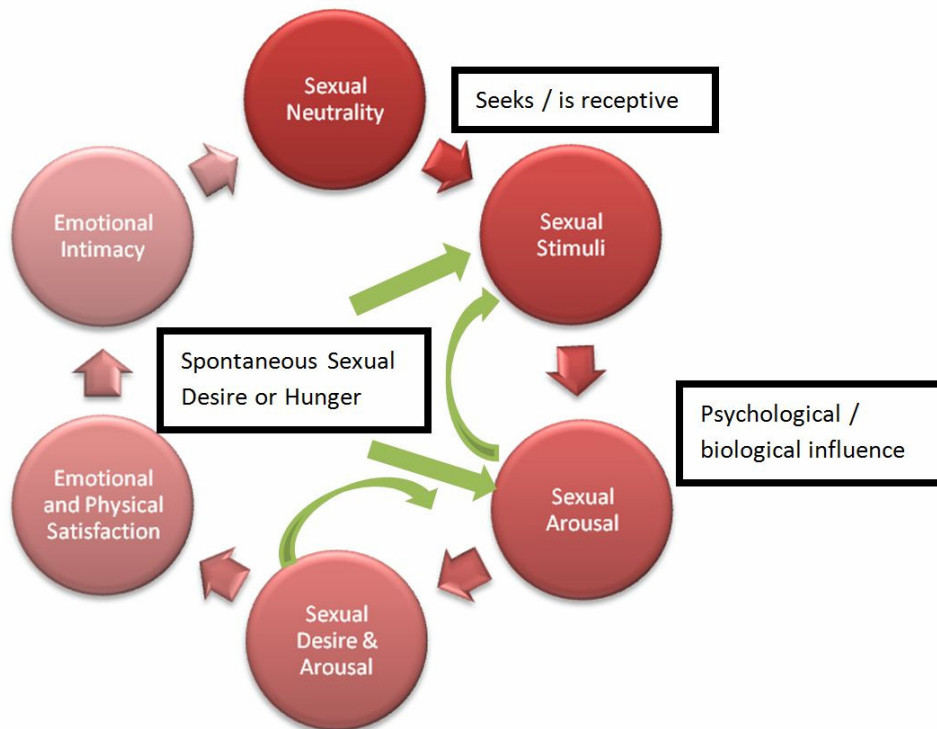
In 1974 Kaplan modified the model by including the importance of sexual desire (figure 2).

Figure 2 Linear model of human sexual response including desire. Kaplan HS. J Sex Marital, 1979;3:3



In 2001 Basson introduced a circular model regarding both women and men, where the importance of mental well-being, psychological and biological factors was included. From a stage of sexual neutrality, letting sexual stimuli arouse us, we can experience sexual desire which then enhances sexual arousal and thereby achieving emotional and/or physical satisfaction (figure 3) (6).

Figure 3 Circular model of human sexual response. Adapted from Basson R. Journal of Sex & Marital Therapy.2001, 27:395-403.



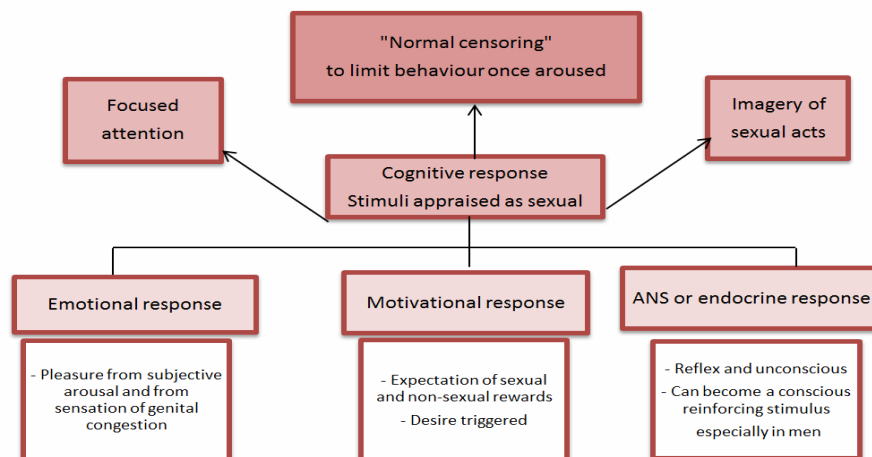
In a study Sand and Fisher assessed which of the three sexual response models is the most accepted by women (6). The linear model (figure 2) was found to best apply to both women and men with normal sexual function. Whereas the circular model was found to be most applicable for women with Female Sexual Dysfunction (figure 3). The model shows the complexity in womens sexual response and in how many ways it can be affected.

Sexual arousal

Sexual arousals consist of the mind processing internal stimuli (e.g. fantasy) coupled with external sexual stimuli. Using Positron Emission Tomography (PET) for brain imaging during visual sexual stimulation identifies a model of sexual arousal that includes several areas of the brain (cortical, limbic, and para-limbic) that are known to be associated with cognitive function, motivation, and emotions, linked to changes within the autonomic nervous system (figure 4). However, there is a difference between men and women. Men can assess their own genital engorgement which correlates with subjective arousal and encourages further arousal. Whereas in women, the correlation between the subjective arousal and measures of increased vaginal congestion and clitoral blood flow is minimal for most women (1).

It is worth to notice that the word "arousal" may cause confusion in my thesis, because it is used in both sexology and in sleep medicine, but with entirely different meanings. In a sexual context, arousal is a positive and desirable phenomenon. In sleep medicine, arousal is a disturbance of sleep, defined by change in sleep EEG. This causes a deterioration of sleep quality, and is therefore undesirable.

Figure 4 Model of sexual arousal. Adapted from Basson R. and Schultz WW. Sexual Dysfunction 1. Lancet 2007;369:409-24.



The difference between women and men is rather obvious from the questionnaires used when sexuality is investigated. Furthermore, in women you often use two questionnaires because the sexual function is split into two: one investigating if there are any sexual difficulties, and one investigating if there is any sexual distress. Only if both sexual difficulties and sexual distress are present does the patient suffer from sexual dysfunction (7;8). In order to demonstrate sexual dysfunction, you may use “cut off” scores in both sexual function and sexual distress.

When initiating these studies I did not find any questionnaire specifically focusing on sexual distress in men. The Brief Sexual Function Inventory (BSFI) has three questions addressing whether or not the participant considers erection, ejaculation or desire to have been a problem for them in the past 30 days. In 2007, just after the start of my study, the Italian Society of Andrology designed a self-administered ad-hoc questionnaire investigating sexual distress in men, the Sexual Distress Evaluation Questionnaire for Men (SDEQ-M)(40). They found that sexual distress is present in 29 % in male patients attending sexual medicine clinics. One may speculate that the male patients in this study would had shown an equal percent of sexual distress if we had had the opportunity to measure it.

SLEEP

Sleep has always been a mystery and still is. In ancient times sleep was considered to resemble a death-like state. Bertel Thorvaldsen's beautiful relief: The Angel of the Night with her children Hypnos (Sleep) and Thanatos (Death) (figure 5) shows how sleep and death were perceived as twin brothers. However, modern science has shown differently. Today we know that even though sleep is a state of body rest, the brain is very active and sleep is mentally and physiologically a most important “prerequisite” for a healthy life.

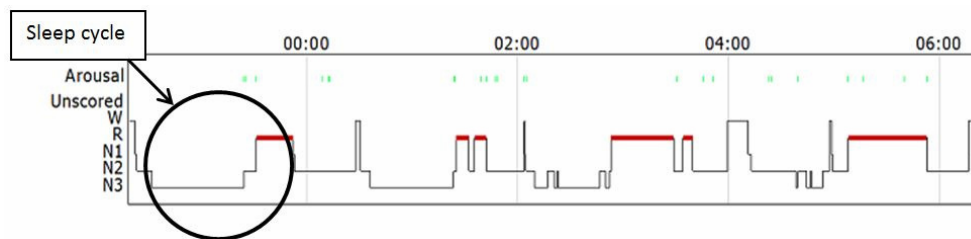
Figure 5 Bertel Thorvaldsen's relief from 1815 shows The Angel of the Night with her twins Hypnos and Thanatos, Sleep and Death.



Sleep stages

Sleep is divided into four stages: N1 – dozing, N2 – light sleep, N3 – deep sleep (slow-wave sleep) and in addition dream sleep/ rapid eye movement (REM). Furthermore stage N1 – N2 – N3 are called Non Rapid Eye Movement (NREM). N1 – N2 – N3 + REM sleep are included in a “sleep cycle”, which takes about 90 minutes and repeats 4 – 6 times through the night (figure 6). Normally NREM predominates the first part of a sleep period. During NREM production of several hormones peak; i.e. growth-, sex, and metabolic hormones. REM predominates found in the latter part of the sleep period and is normally characterized by lack of muscular tone except for specific eye-movements and engorgement of genitalia. The latter is more obviously in men than women.

Figure 6 Hypnogram showing the sleep stages of a normal (adult) sleep. REM sleep is marked in red.



Sleep disturbances

Numerous sleep disorders e.g. insomnia, upper airway resistance syndrome (UARS), obstructive sleep apnea (OSA), narcolepsy, periodic leg movements during sleep (PLMS) or restless legs (Restless Legs Syndrome - RLS) result in disturbances of the quality of sleep. This may cause daytime sleepiness and hypersomnia and have negative cardiovascular and metabolic effects.

Polysomnography (PSG) is a clinical neurophysiological method for the investigation of sleep and the changes occurring during sleep. The recording montage includes electroencephalography (EEG), electromyogram (EMG),

airflow, oxygen saturation, respiratory effort, electrocardiogram (ECG), and eye movements (electrooculogram). Because the access to full polysomnography has been restricted due to its cost and limited availability, the standard for investigation of OSA often is a simplified technique that focuses on respiratory parameters, usually not including EEG. The measurement includes two belts located around the abdomen and chest recording the respiratory movements. A nasal catheter records the air flow. An oximetry probe on a finger measures heart rate and the oxygen saturation. The sensors are attached to a small recording device usually attached to the body.

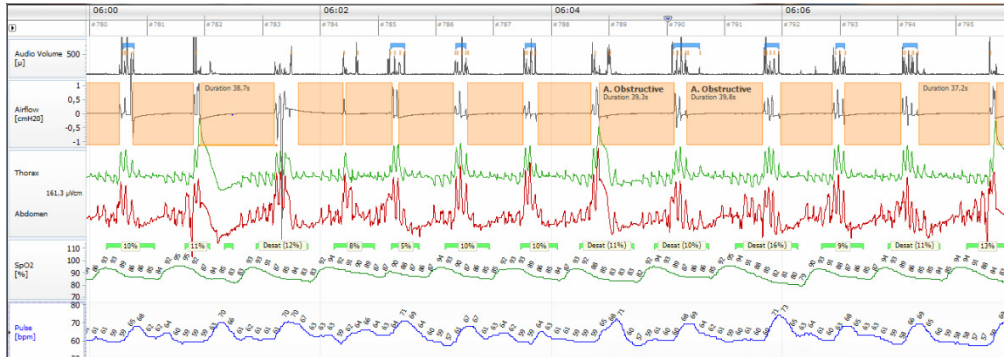
Obstructive Sleep Apnoea

OSA is defined as repetitive partial or complete cessation of breathing (hypopnoea/apnoea) during sleep due to upper airway collapse. Apnoeas are diagnosed as cessation of breathing lasting more than 10 s. Hypopnoeas are diagnosed as a reduction in airflow associated with a desaturation of at least 3% or 4%. The severity of OSA must be examined in order to make an appropriate treatment decision. The examination will include objective as well as subjective information such as medical history, scores of daytime sleepiness and quality of life.

The number of hypopnoea/apnoea during sleep is given as Apnoea Hypopnoea Index (AHI) indicating the severity of OSA: an AHI < 5 is normal, AHI 5-15 is considered mild sleep apnoea, AHI 15-30 moderate sleep apnoea and AHI > 30 severe sleep apnoea. In 2009 the Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine (AASM) designed a guideline to assist therapists who treat patients with OSA (9). In the guideline AASM underline the importance of the subjective information: Unintentional sleep episodes during wakefulness, daytime sleepiness, unrefreshing sleep, fatigue, insomnia, waking up choking, breathing interruptions.

When an apnoea caused by an obstruction appears, the patient will struggle to breathe again. Movements of thorax and abdomen will occur but no air flow will be present, normally resulting in a desaturation at the end of the apnoea as shown in figure 7.

Figure 7 Sleep apnoea recording, showing the respiratory flow with repetitive apnoeas. Traces from top to bottom: Audio recording of snoring. Airflow. Movement of thorax and abdomen showing paradoxical breathing when the patient struggles to breathe. Saturation-curve with a saw-tooth pattern of desaturation. Pulse-curve showing bradycardia during apnoeas.



Another sleep respiratory disorder is called central apnoea where the breathing stops and there is no movement of thorax or abdomen. The clinical presentation of central apnoea is different from that of OSA, although both types of apnoeas may be found in the same sleep recording.

Risk factors

The reasons for OSA are manifold. For example; narrow upper airways, reduced muscle tone in the upper airways or hypertrophied tonsils and adenoids. Not all physicians have the possibility to examine the patients' upper airways. Accordingly AASM suggests five questions that should be included in routine health maintenance evaluation: Is the patient obese? Is the patient retrognathic? Does the patient complain of daytime sleepiness? Does the patient snore? Does the patient have hypertension?

The main risk for developing OSA is obesity especially if narrow upper airways are present as well (10). Also AASM emphasizes the presence of obesity, signs of upper airway narrowing, or the presence of other disorders that can contribute to the development of OSA. Several studies have found that untreated OSA may lead to hypertension, angina pectoris or/and myocardial infarction and furthermore

reported a doubled risk for stroke or cardiovascular death (11;12). Table 3 shows the list of patients at high risk for OSA.

Table 3 Patients at high risk for OSA who should be evaluated for OSA symptoms. (12).

Obesity (BMI > 35)
Congestive heart failure
Atrial fibrillation
Treatment refractory hypertension
Type 2 diabetes
Nocturnal dysrhythmias
Stroke
Pulmonary hypertension
High-risk driving populations
Preoperative for bariatric surgery

Symptoms

The consequences of OSA are present at night as well as during the day. At night symptoms may include nocturia, frequent awakenings, a sensation of choking, sweating and reflux. Daytime symptoms may include sleepiness, drowsiness, morning headaches, decreased libido, concentration difficulties, learning difficulties, irritability and depression.

Approach

OSA should be approached as a chronic disease and thus requiring long-term treatment. The effects of the treatment of OSA should be monitored closely to ensure optimal treatment. Follow-up should be once a year. If changes occur such as weight loss $\geq 10\%$ of body weight, the patient should be examined for modification of the treatment. Education of the patient about the function and care of their equipment, the benefits of the treatment and potential problems has great value for the success of the treatment. AASM have listed components of an education program (table 4).

Table 4 Components of patient education program. (9).

Findings of study, severity of disease
Pathophysiology of OSA
Explanation of natural course of disease and associated disorders
Risk factor identification, explanation of exacerbating factors, and risk factor modification
Genetic counseling when indicated
Treatment options
What to expect from treatment
Outline the patient's role in treatment, address their concerns, and set goals
Consequences of untreated disease
Drowsy driving/sleepiness counseling
Patient quality assessment and other feedback regarding evaluation

There are several treatment options for OSA. AASM divides the options into two: Continuous Positive Airways Pressure (CPAP) and alternative therapies, which include behavioural (weight loss, exercise, positional therapy, avoidance of alcohol and sedative before bedtime), oral appliances (improving upper airway patency during sleep), surgical (upper airway reconstruction or by-pass procedures, often site-directed and /or staged) and adjunctive therapy (bariatric surgery, medication, oxygen). CPAP is chosen for moderate and severe OSA and in some cases for mild OSA. It is important that the patient is an active part in the decision of treatment, to manage and comply with the CPAP-treatment. In this thesis CPAP is the only treatment studied.

Obstructive sleep apnoea and sexuality

A number of factors that influence sexuality can be found in people with poor sleep. Fatigue, irritability and depression are commonly observed in patients with OSA, and may be part of the factors known to have influence on sexuality (Table 1). OSA is considered to be part of the metabolic syndrome (diabetes, hypertension, obesity) where sexual problems are commonly seen. The reason may be functional or structural vascular disorder. Treating OSA may also have effects on decreased sexual function. Some patients will experience improvement and others may not, depending on whether or not their sexual problems are primary or secondary. Primary sexual problems can be exemplified by vascular problems, secondary can be caused by fatigue. If the sexual problem is primary, the treatment of OSA will have little if any influence, which is why patients with this kind of problem should be referred to a sexological clinic or similar, for appropriate treatment. If the problem is secondary, amelioration of general sleepiness with CPAP treatment may well improve sexual function.

In couples where one partner has a chronic disease, sexuality will often be affected. This affects not only the patient, but also the partner. The partner may try to show consideration, but this may inadvertently result in moderation, rejection and insecurity regarding closeness and sexuality, resulting in a negative self-reinforcing sexual function. The circular model of human sexual response (figure 3) shows how both the patient and the partner can be affected, and underlines that the couple is exposed to sexual difficulties.

CPAP-treatment

The CPAP device consists of a machine that generates a positive pressure and a tube connecting the CPAP machine to a mask which the patient has to wear during sleep (figure 8). The mask may cover the nose (nasal mask) or mouth and nose (full-face mask).

Figure 8 CPAP device, tube and nasal mask



A well-fitting mask is very important. If the mask is too loose leaks may occur and if the mask is stretched too tightly it may result in pressure ulcers. To prevent drying out of the mucosa in nose and throat, it is possible to connect a humidifier to the CPAP device. Auto-CPAP devices are commonly used because of their ability to automatically adjust the pressure delivered. The necessary pressure may change through the night, depending on body position and sleep stage. Regular follow-up of treatment by qualified personnel is important to maximize patient compliance with CPAP treatment.

Information about any evidence-based positive effect of CPAP treatment e.g. in relation to sexuality may help to increase acceptance of CPAP therapy.

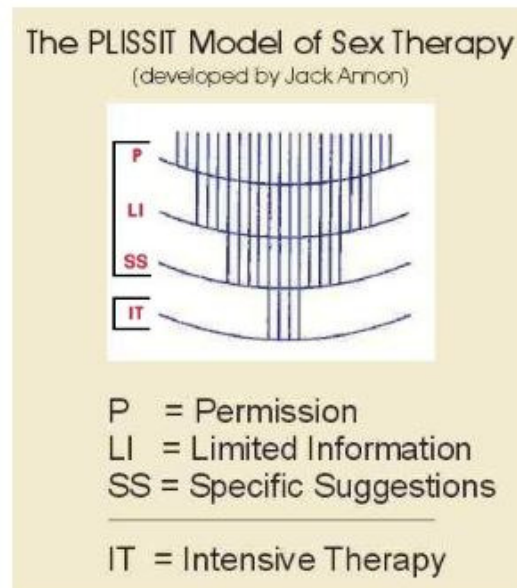
Education

To achieve optimal compliance with CPAP treatment, one has to educate and inform the patient and if possible the partner as well, furthermore discuss treatment goals and expectations. Treatment with CPAP is very much an intrusion of the bedroom. There may be practical issues concerning the placement of the CPAP device as well as cleaning the parts of the mask and device requires time and space. Especially in the beginning, the sound from the CPAP machine and leaks around the mask may be troublesome for both patient and partner. It takes time and experience to get optimal compliance, which is why it can be crucial that both patient and partner have knowledge of the disease, the consequences of untreated OSA and the expected results of the treatment.

The responsibility to ask about and to discuss sexual difficulties must reside with the therapist. If a patient does not bring up sexuality it does not mean that there are not problems. The initiating of CPAP treatment often takes place in clinics (i.e. ear nose and throat departments, pulmonary clinics) where sexuality is seldom discussed with the patients. There may be a number of excuses for the therapist not bringing up the topic: "If the patient has a problem I am sure he/she would bring it up", "It is too embarrassing for the patient to talk about sexuality", "I do not have the time to bring up sexuality in the consultation", "Surely he/she does not have sex at this age", "It is outside my competence".

I think the only one who may be embarrassed is the therapist. The patient does not expect you to be a professional sexologist, but just asking about the topic can reassure them that he/she is not the only one who may have difficulties with sexuality. The American sexologist, Jack Annon showed in a model called PLISSIT the several levels for talking about sexuality (figure 9). When using this model, the first levels will be possible for all therapists to deal with.

Figure 9 PLISSIT model by Annon JS and Robinson CH (1978).



P stands for **Permission**, since many sexual problems are caused by anxiety, guilt feelings, or inhibitions. It follows that a therapist who, using his professional authority, simply "gives permission" to do what the patient is already doing, can alleviate much unnecessary suffering. (Example: Guilt feelings and anxiety because of masturbation)

The next step of therapeutic intervention is called **LI** or **Limited Information**. Often it is enough to give patients correct anatomical and physiological information to restore their sexual functioning. It is not at all uncommon that patients have erroneous notions about the functioning of their own body and thus fall victim to unrealistic expectations. In such cases little more than factual information and education is necessary.

The next step - **SS**, **Specific Suggestions**, requires practical hints or exercises tailored to the individual case. Many of the exercises of mutual pleasuring recommended by Masters and Johnson belong in this category.

Only the last step - **IT** or **Intensive Therapy**, requires a long-term intervention addressing complex underlying causes. Annon is convinced, however, that these cases are relatively rare.

PRESENT STUDY

Aim of the thesis

The overall aim of this thesis was to study the impact of nocturnal CPAP treatment on sexuality and closeness in patients with obstructive sleep apnoea.

The specific aims were:

- Paper I: To investigate general and functional aspects of sexuality in male patients with a confirmed diagnosis of Obstructive Sleep Apnoea (OSA) and compare the results to normative data.
- Paper II: To investigate sexual dysfunction and sexual distress in female patients with obstructive sleep apnoea and to determine which factors are of importance to their sexual function.
- Paper III: To investigate what impact one year of effective nocturnal CPAP treatment has on general and functional aspects of sexuality in male patients with a confirmed diagnosis of Obstructive Sleep Apnoea (OSA).
- Paper IV: To describe the impact of CPAP treatment on sexual difficulties and sexual distress in female patients with OSA after one year on treatment.

Material and Methods

Paper I & II Patients (male n=308, women n=92) with OSA were consecutively recruited from patients assessed in three sleep laboratories of one sleep clinic (ScanSleep) in Denmark from October 2005 to January 2008.

The study comprised only patients ≥ 18 years old, able to read and write Danish and with a diagnosis of OSA [apnoea-hypopnoea index (AHI) >5] requiring treatment with CPAP. The material thus consisted only of patients where CPAP was considered as being the clinically relevant treatment of choice as judged by an experienced specialist. Approximately 90% of the eligible patients accepted to participate. All patients were investigated for OSA using identical portable devices (EMBLETTA®, Embla, Broomfield, CO, USA). The recording montage included nasal airflow using a nasal pressure catheter, respiratory movement with thoracic and abdominal bands (XactTrace, Embla, Broomfield, CO, USA), pulse oximetry and body position. Apnoeas were diagnosed as cessation of breathing more than 10 s. Hypopnoeas were diagnosed as reduction in airflow $> 30\%$ associated with a desaturation of 4% or more. The number of apnoeas and hypopnoeas/hour (AHI) was calculated on estimated sleep time (as reported by the patient) as the denominator. Data of self-reported daytime sleepiness were collected using the Epworth Sleepiness Scale (ESS). The ESS assesses the likelihood of the patient dozing off or falling asleep in eight daily situations using a score between 0 and 3. The maximum score is thus 24, with a score of 11 or more being taken to indicate significant levels of daytime sleepiness (13).

For both genders data on sexual function in general and closeness were obtained using the Fugl-Meyer Life satisfaction checklist (LiSat-11) (14). After personal communication with the author of the questionnaire asking which questions could be used to investigate closeness we used four questions: Life as a Whole and three domains of closeness (Sexual Life, Partner Relationship, Family Life. The referent population consisted of both sexes, but we used data specific for each gender received from Fugl-Meyer (A. Fugl-Meyer, pers. comm.). Satisfaction was scored on a scale from 1 to 6, with higher scores indicating greater satisfaction.

Socio-demographic data on age, body mass index (BMI), marital status and education were collected for all individuals, and their current use of medication was recorded as a proxy for comorbidity.

Specific sexual questionnaire for men was the Brief Sexual Function Inventory (BSFI) (15) in which the first 10 items cover functional aspects of male sexuality during the past 30 days: Sexual drive and level of sexual drive (two items), partial or full erection, capability to intercourse and difficulties in getting erection (three items), difficulty ejaculating and satisfaction with the amount of semen (two items) and problem assessment concerning sexual drive, erection and ejaculation (three items). The last item covers overall sexual satisfaction and consists of one question. The items were scored from 0 to 4, with higher scores indicating better function. The total score was

calculated for the first 10 items. Item 11 (overall satisfaction) is not a functional question and was therefore analyzed separately, and not included in the statistical analyses for total score.

No control data on Fugl-Meyer LiSat-11 or on BSFI has been reported for the male Danish population. We therefore used summarized normative male data from Sweden and Norway since they are countries linguistically, culturally and sociologically closely related to Denmark. From Sweden, Fugl-Meyer LiSat-11 data were collected by questionnaires and face-to-face interviews, and participants were drawn from the Swedish Central Population Register (14) and from Norway (for BSFI) participants were recruited by using public address lists and sending questionnaires (16).

Specific sexual questionnaires for women were Female Sexual Function Index (FSFI) and Female Sexual Distress Scale (FSDS). FSFI is a validated 19 items measure of female sexual function for women with a sexual partner. The 19 items are assigned to six domains: Desire (two items), arousal (four items), orgasm (three items), pain (three items), vaginal lubrication (four items), and sexual satisfaction (three items). Higher scores indicate better sexual function (17;18). FSFI has a score ranging from 2 to 36. The scores can be dichotomized with a cutoff at 26.55 differentiating women with and without sexual difficulties. When scoring ≤ 26.55 , the respondent is likely to have a sexual difficulty (19). FSDS consists of 12 validated questions measuring sexual-related personal distress in women. The distress is scored on a scale from 0 to 4 for each item, with higher score indicating higher distress. The total range of the scale is 0–60. FSDS scores can be dichotomized with a cut-off score at 15. Scoring ≥ 15 indicates sexual distress [18]. Manifest Female Sexual Dysfunction (MFSD) is present when the respondent has both sexual difficulty (FSFI ≤ 26.55) and sexual distress (FSDS ≥ 15)(7;8).

The women used as controls were participants from a cross-sectional national survey of Danish women's sexual life. A total of 1,996 Danish women were identified from the central health registry. Criteria for selection were age 20–65 years and zip codes ensuring that the group reflected the population with regard to which part of the country they lived in. The women were mailed the questionnaires. From the respondents, we selected 240 women age-matched to the OSA group - three from the control group for each OSA patient and included their raw data in our analyses. Data on age, BMI, permanent sexual relationship, and education were collected for both patients and normal subjects. Menopause was considered a more relevant variable than age per se, but because menopausal state was not known for all subjects, we subdivided the material according to age with a cut-off value of 45 years as a proxy for

menopause. BMI was also analyzed as a dichotomous variable with BMI ≥ 30 as the obesity limit.

Paper III. Three hundred and eight male patients were included in the baseline study. Of these, 267 (87%) were continuing with CPAP after one year. Because of technical reasons and coding of the questionnaires 51 patients were lost to the one year follow up. The remaining follow up cohort of 207 patients were given or sent the follow up questionnaires; of these 157 (76% response rate) returned the forms.

Paper IV. Ninety-two female patients aged 22 to 71 years were included in the baseline study. Of these, 54 (59%) were still using CPAP after one year. These patients were given or sent the follow up questionnaires. Forty four (81% response rate) returned the forms.

STATISTICAL ANALYSIS

Paper I. Descriptive statistics [mean and standard deviation (SD)] were used to summarize the clinical and socio-demographic data. A power analysis with respect to the 6-point scale Fugl-Meyer LiSat-11 showed that 80 patients would be sufficient to demonstrate with 95% certainty a difference between normal and patients of 0.5 points at the 0.05 one-side significance level, assuming that the patients had the same SD as the normal subjects. Regression analysis was performed for the Fugl-Meyer LiSat-11 and BSFI, to assess the specific impact of BMI, AHI, ESS, being in a relationship, education, employment and medication. T-tests were used when comparing study data with reference subjects based on available data for n and SD. A significance level of $P \leq 0.05$ was used for all statistical analyses.

Paper II. Descriptive statistics (mean and standard deviation [SD]) were used to summarize the clinical and anthropometric data. For descriptive purposes, Student's t-tests and chi-square test were used when comparing study data to reference subjects. The first statistical step was to apply Pearson's correlation

to relate FSFI, FSDS, and MFSD to age, BMI, OSA, AHI, ESS, cardiovascular medication, psychopharmacology, antidiabetics, and education. Based on the results from the correlation analysis, we decided to include age, BMI, and the use of psychopharmacology in the next step which was multiple regression analyses with FSFI, FSDS, and MFSD as the dependent variables. Because of the focus on OSA in this article, we included AHI in the analyses for OSA patients although no correlation was found in the correlation analysis. A significance level of $P \leq 0.05$ was used for all statistical analyses.

Paper III. We applied multiple regression analysis to difference (Δ) in LiSat-11 and Brief Sexual Function Inventory (BSFI) before and during CPAP treatment to assess any impact of Age, BMI, ESS, regular partner, education, employment and medication at baseline. Regression analysis was also performed to see if the changes in LiSat-11 and BSFI were dependent on the changes in ESS. Paired t-tests were used when comparing study data before and during CPAP treatment. A significance level of $p \leq 0.05$ was used for all statistical analyses.

Paper IV. Descriptive statistics (mean and standard deviation [SD]) were used to summarize the clinical and socio-demographic data. Paired t-tests were used when comparing numerical study data before and during CPAP treatment. McNemar Test (for changes in proportion of categorical data) was used when investigating the changes in FSFI (cut off ≤ 26.55), FSDS (cut off ≥ 15) and MFSD. All tests were performed in the total group but also for the subgroups < 45 years old and ≥ 45 years old. A significance level of $p \leq 0.05$ was used for all statistical analyses.

SUMMARY OF RESULTS

Men, paper I and paper III

Paper I. We found that both general (LiSat-11) and functional (BSFI) aspects of sexuality were worse in patients with (untreated) OSA when compared with normative data. Both aspects were dependent on age, obesity, social factors and concomitant medication but not on the severity of OSA as reflected by the apnoea-hypopnoea index or subjective sleepiness (ESS).

Paper III. We found no significant changes in Life Satisfaction with Relation to Partner or Life as a Whole, but satisfaction with Sexual Life (Li-Sat 11) and both general and functional aspects of sexuality (BSFI) were significantly improved after 1 year of CPAP treatment. Epworth Sleepiness Scale (ESS) score decreased significantly after 1 year of CPAP treatment.

Figure 10 shows the changes regarding Life Satisfaction 11 within the OSA group. Figure 11 shows changes regarding Brief Sexual Function Inventory within the OSA group.

Figure 10 LiSat-11. Changes within the OSA group.

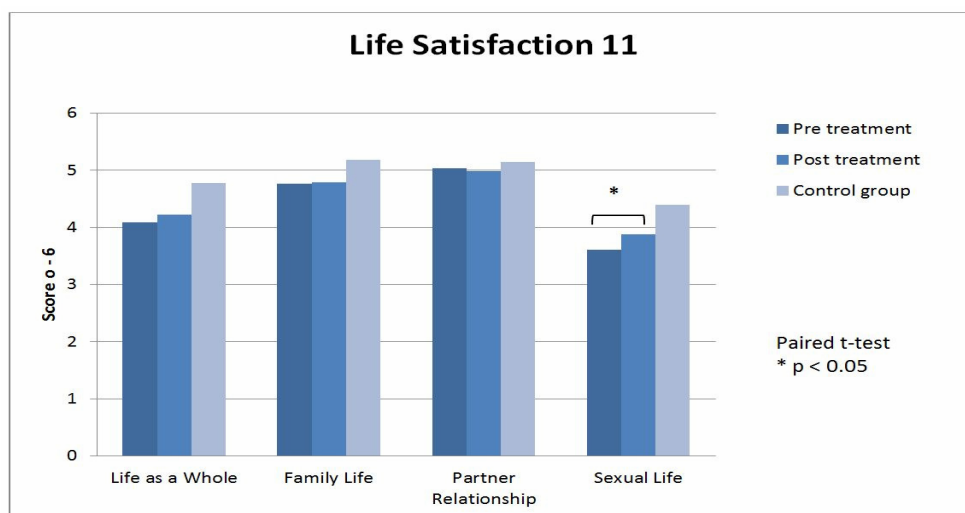
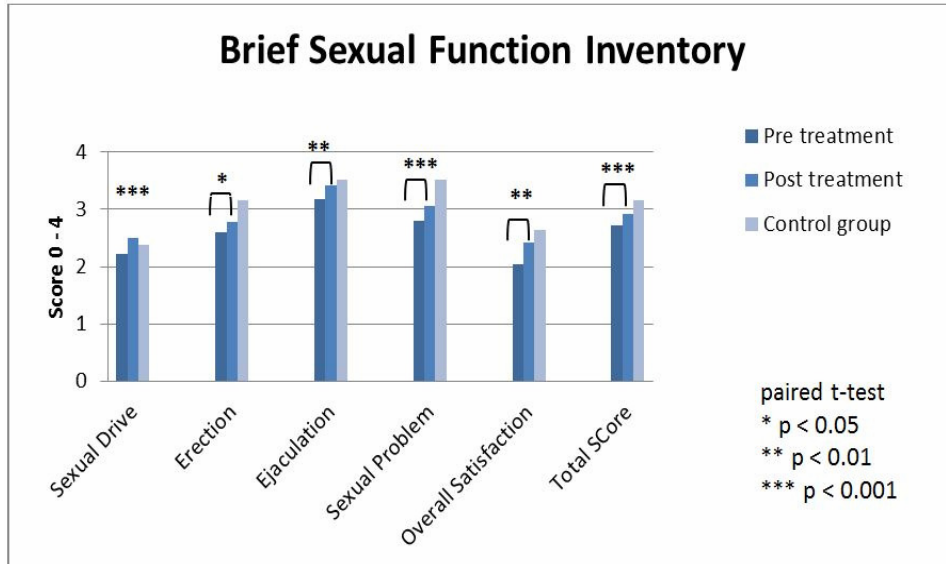


Figure 11 BSFI. Changes within the OSA group.



Women, paper I and paper III

Paper II. Female Sexual Function Index indicated that obstructive sleep apnoea patients were at a higher risk for having sexual difficulties. Female Sexual Distress Scale showed significantly more sexual distress in the obstructive sleep apnoea group. Manifest Female Sexual Dysfunction (combined data from Female Sexual Function Index and Female Sexual Distress Scale) showed that female patients with obstructive sleep apnoea also had more sexual dysfunction. Severity of sleep apnoea was, however, not related to any of these indices, but consumption of psychopharmaca was. In Lisat-11, we found that female patients with obstructive sleep apnoea scored lower than women in the population sample regarding Life as a Whole.

Paper IV. We found a significant positive change in Manifest Female Sexual Dysfunction (figure 12), but no significant changes in isolated sexual difficulties (figure 13) or sexual distress (figure 14). Daytime sleepiness decreased significantly after one year. The results from the questionnaire LiSat-11 were unchanged after one year. In addition the distribution of the normative group is included in the figures below.

Figure 12 Manifest Female Sexual Dysfunction (MFSD) (n = 32 only patients with regular partner) shows significant positive change pre- vs. post-treatment. McNemar Test * p = 0.04.

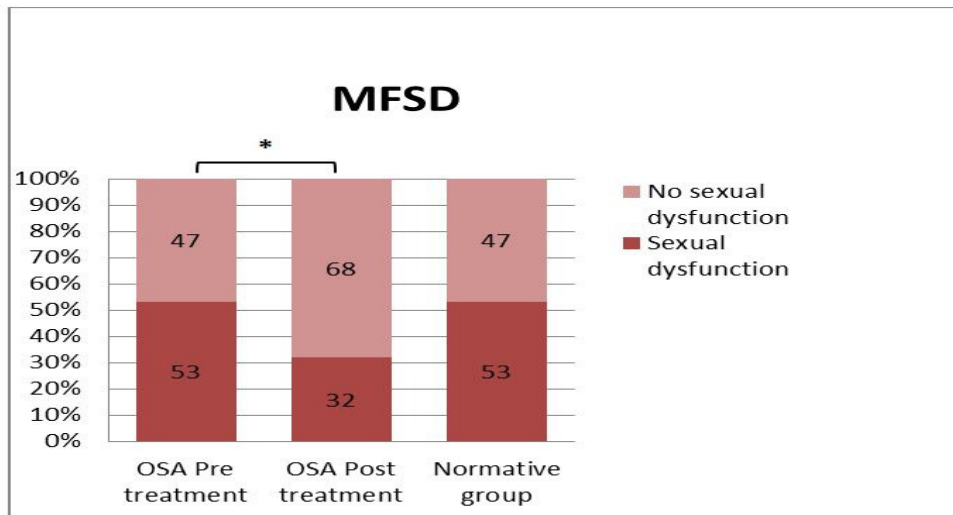


Figure 13 Female Sexual Function Index (FSFI) (n = 32 only patients with regular partner) shows no significant positive change pre- vs. post-treatment. McNemar Test.

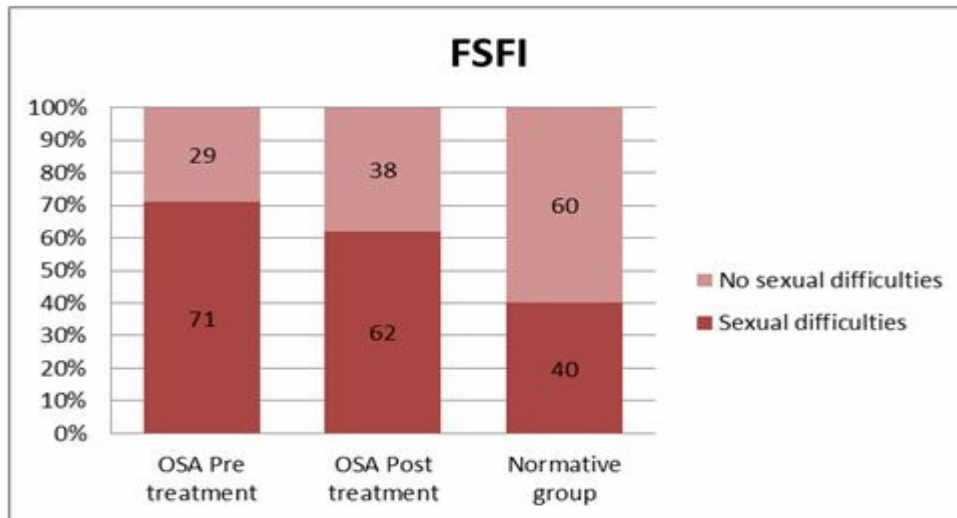
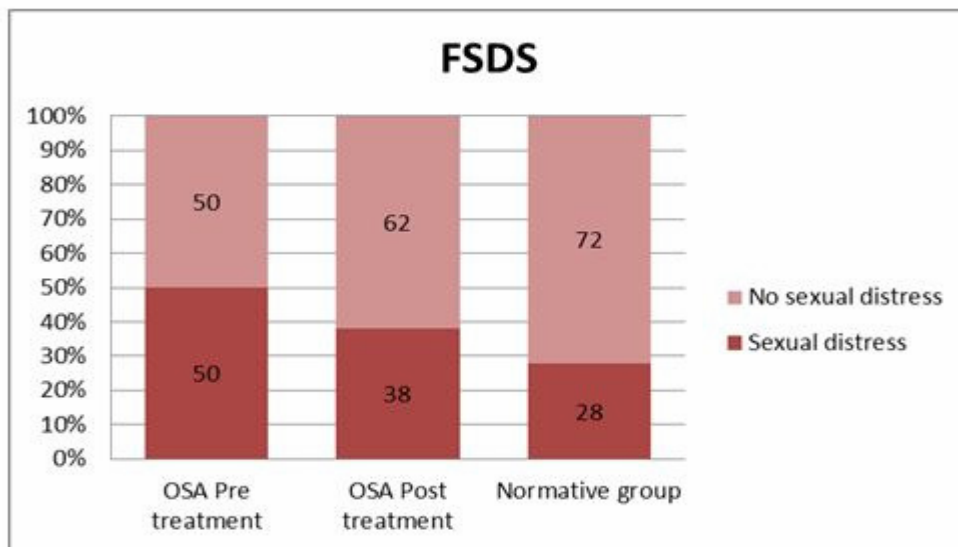


Figure 14 Female Sexual Distress Scale (FSDS) (n = 44) shows significant positive change pre- vs. post-treatment. McNemar Test.



GENERAL DISCUSSION

Choice of questionnaires

When deciding which questionnaires to use in the study several aspects had to be considered. Which sexual questionnaires were evaluated and relevant? And which questionnaires were translated into Danish. Eventually we identified three relevant questionnaires. One specifically for men, the Brief Sexual Function Inventory (BSFI) (17) and two for women Female Sexual Function Index (FSFI) (18,19) and Female Sexual Distress Scale (FSDS) (20).

The BSFI measures 11 items during the past thirty days. The first ten items cover functional aspects of male sexuality and the last item covers general satisfaction. The scores are given in mean and SD. There was no Danish control group, why we used a control group from our comparable Nordic neighbour, Norway.

For women we used the FSFI and FSDS and a large Danish normative group was available. The scores in the questionnaires are shown in mean and SD, but it is also possible to use a cut-off. When using a cut off you are able to demonstrate Manifest Female Sexual Dysfunction (MFSD), which is only present when the respondent has *both* sexual difficulty ($FSFI \leq 26.55$) and sexual distress ($FSDS \geq 15$) (7;8).

The Female Sexual Function Index (FSFI) is a 19 item, multidimensional, self-report questionnaire used to measure sexual function. FSFI has a score ranging from 2 to 36. The scores can be dichotomized with a cutoff at 26.55 differentiating women with and without sexual difficulties. When scoring ≤ 26.55 , the respondent is likely to have a sexual difficulty. FSFI is a strong and exact measure to describe female sexuality, but is limited to participants with a partner. Accordingly it could not be used in 25% of the female patients, who were single. This is a weakness in my study, since information on sexual difficulties is missing on singles.

The Female Sexual Distress Scale (FSDS) is a 12-item self-report questionnaire to measure sexually related personal distress in women. The distress is scored on a scale from 0 to 6 for each item, with higher score indicating higher distress. Scores above the cut off ≥ 15 represent sexual distress.

For both genders we used the Life Satisfaction 11 (Lisat-11) and Epworth Sleepiness Scale (ESS).

Life Satisfaction 11

From LiSat-11, which consists of 11 questions, we used four questions concerning general satisfaction with life: Life as a Whole and three items of closeness (Sexual Life, Partner Relationship, Family Life). The epidemiological validity of LiSat-11 is based on a random sample of 5250 women and men aged 18 – 74 drawn from the Swedish Central Population Register.

These data were originally reported combined for men and women (14) However, I received raw data from Dr. Axel Fugl-Meyer (personal communication), making it possible to separate data for men and women and using the sample as normal controls. Dr. Fugl-Meyer has included the item “Sexual Life” into the domain of closeness. It have be questioned whether this is relevant when describing closeness, as sexual life not necessarily adheres to closeness. However, I have chosen to follow the outline of Dr. Fugl-Meyer, as the item is of value in future comparative studies in men and women.

Epworth Sleepiness Scale

ESS is one of the most used questionnaires assessing daytime sleepiness. ESS assesses the likelihood of the patient dozing off or falling asleep in eight daily situations using a score between 0 and 3. The maximum score is thus 24, with a score of 11 or more being taken to indicate significant levels of daytime sleepiness. Through time the validity of ESS has been questioned and a number of studies show misfit in some of the items (13).

Men: Paper I and paper III

Paper I is investigating general sexual activity and functional sexual aspects in patients with a confirmed diagnosis of OSA compared with age-matched controls. Most other studies focus on (self-reported) erectile function, whereas the present study also deals with self-reported sexuality in a wider context. Our results show that male patients with OSA score worse than the control groups, not only on questions regarding health in general but also on questions regarding general and specific aspects of sexuality.

It is difficult to draw any firm conclusions concerning the true prevalence of co-morbidities from the data concerning cardiovascular or psychopharmacological medication. However, it seems that our patients in general have more

cardiovascular co-morbidities. This is in line with other findings, showing an overlap between OSA and not only cardiovascular disease, but also Diabetes Mellitus type II (20;21).

Paper III shows a highly significant improvement of sexual life in general (LiSat-11) and in all aspects of sexual function (BSFI) in male OSA patients after one year of CPAP treatment.

The response rate to the questionnaires was 76% and the majority of the respondents (93%) were CPAP compliant.

In our study we found an improvement of sexuality in general, but we could not find any relationship to specific factors. This is in contrast to Reishtein *et al.* (22) who found a relationship between sexual function and daytime vigilance both at baseline and after CPAP treatment. One explanation for this discrepancy may be that Reishtein and co-workers used the Intimate and Sexual Relationships subscale of the Functional Outcome of Sleep Questionnaire (FOSQ), where the four questions on sexuality refer to the specific impact of sleepiness, whereas the BSFI used in our study is a general sexologic instrument. However Reishtein *et al.* supports our findings with respect to the lack of a relationship between the change in outcome score and pretreatment data for age, BMI and AHI.

We found no significant changes in items of more personal and social perspectives as Life as a Whole, Family life and Partner relationship after one year of effective CPAP treatment, which may indicate that neither partnership nor social status had changed during the period of CPAP treatment. Therefore organic (neural, hormonal and/or vascular) mechanisms remain as the most likely explanation to our findings as shown in other studies as well (23-25). If the sexual distress in our patient-group had been measured using the sexual Distress Evaluation Questionnaire for Men, it would have been interesting to see, if the result followed sexual function and thus improved, or followed the more personal and social perspectives and thus remained unchanged.

Women: Paper II and paper IV

Paper II. Our results confirm observations of previous studies that women with diagnosed OSA have more sexual difficulties and sexual distress than women without OSA (26-28). Our data show that age > 45 years is negatively related to sexual function but not sexual distress. That sexual distress is not negatively affected by age, may reflect that the ability to cope with sexual difficulties improve with increasing age. Similar results have been shown in several studies (26;27;29;30).

We did not have specific questionnaires on depression in our study, but we found a significant relationship between the use of antidepressants and sexual difficulties as well as sexual distress, within the OSA group. As shown in earlier studies (31),(32), depression may play a major role in female sexuality. Shifren *et al.*(33) found an increased incidence (odds ratio [OR] 2.4) of depression in patients with sexual distress. Depression has shown to have an impact on sexual function in other chronic illnesses, and screening for depression is suggested in all patients with chronic illness and sexual dysfunction (30;34;35)

Scores from Li-Sat 11 shows general dissatisfaction with Life as a Whole in OSA women, but no difference to the population sample concerning domains of closeness (family life, partner relationship and sexual life). This is in contrast to our study in men (36). We speculate that women, to a larger degree than men, tend to see family life and sexuality entities separate from well-being. On the other hand, well-being has been shown to be an important factor for female sexual satisfaction (41;42), and Hartmann *et al.* (37), suggests five factors that may interact: age, quality and age of partnership, menopause status, sexual experience and mental health, and personality factors.

Our findings stress the importance of investigating both sexual function and sexual distress regarding female sexuality. I believe it is relevant to clarify potential sexual problems and explain to the patient how CPAP treatment may or may not affect sexuality.

Paper IV shows a beneficial effect of CPAP on Manifest Sexual Dysfunction, but not on sexual difficulties or sexual distress, even though we found a trend ($p = 0.06$) in FSDS. At baseline we considered 92 female patients being a sufficient number for the study. However, at the one-year follow-up only 44 remained in the study and for statistical analysis of sexual function only 32 qualified. One may speculate if the explanation for the lack of improvement in FSFI and FSDS is an Error 2. We therefore did a hypothetical analysis extrapolating the number of our patients to the number at baseline ($n = 92$). With this number of patients assuming the same proportions of responses we would find a significant improvement in FSFI as well as FSDS. This suggests that we do have a type 2 error, and that a larger number of patients might had changed outcome towards improved sexuality in women after CPAP treatment.

When investigating closeness in Lisat-11 (Family Life, Partner Relationship and Sexual Life) we found no significant changes. The score at baseline was equal to the control group. As no changes were found we conclude that CPAP treatment does not affect closeness, which may be of concern to the patient when starting CPAP treatment.

General

The results of the present investigations show that CPAP treatment of OSA affect sexuality differently in men and women.

Sexual function and Sexual Life (LiSat-11) improved in men, whereas in women only reduction of manifest sexual dysfunction (when both sexual difficulty and sexual distress are present) could be shown. CPAP treatment did not affect closeness in neither men nor women and in both genders daytime tiredness decreased. The results underline the importance of knowledge and understanding of sexuality - similarities and differences - in both men and women and that information on possible beneficial effects of CPAP on sexuality may improve early acceptance and long-term compliance of CPAP treatment.

CONCLUSION AND FUTURE RESEARCH

ESS improved significantly, indicating a positive effect on daytime sleepiness. The magnitude of this effect was similar for men and women. Thus we confirm that CPAP treatment decreases daytime sleepiness.

Sexuality improved both in, general and specific aspects in male patients, which is in contrast to female patients in whom only sexual dysfunction decreased . To avoid misunderstanding, we consider it very important to be aware of the gender of the patient when assessing their sexual function. Furthermore regarding women, to keep in mind that you have to divide sexual function into difficulties and distress and that only when both are present, is sexual dysfunction considered.

It is important to underline that all patients in our studies (male and female) had identical diagnostic procedures performed and received the same instructions, follow-up and treatment contacts. The strength of our study is that it was sufficiently long to allow for adaptation of CPAP treatment which often takes at least a couple of months. Many patients may be reluctant to use a treatment involving the use of a mask, a tube and machine every night for many years to come.

The study shows that CPAP treatment *per se* does not negatively affect family life or partner relationship. We consider this new knowledge and important information when initiating CPAP treatment.

Future research comparing women and men regarding OSA, sexuality and their compliance of CPAP-treatment may be valuable for advising and guiding the patient. Further research measuring sexual distress in male patients might shed further light on the sexuality of males.

ACKNOWLEDGEMENTS

I wish to express my sincere appreciation and gratitude to all of you who in many ways made this thesis possible. In particular I would like to thank:

Associate Professor Bengt Midgren, my main supervisor, for guiding and supporting me through the scientific training and always keeping track of things.

Associate Professor Søren Berg, my co-supervisor, for being the one who detected and believed the potential in me, for support and being my friend.

Associate Professor Ellids Kristensen, my co-supervisor, for introducing me to the wonderful world of statistics, supporting me and always being there when I needed it.

Lund University and the Department of Respiratory Medicine and Allergology for allowing me to make my thesis in Sweden.

The Sexological Clinic Research Group, in which I have learned a lot.

Anna-Maria Giraldi, MD, Ph.D. for letting me use her collection of normative data.

The late Axel Fugl-Meyer, MD, Ph.D. for giving me access to primary data.

Neil Stanley Ph.D. for advice and linguistic revision.

All my European friends who have supported and encouraged me in my education and research.

My former (Respiratory Center East) and present (Multidisciplinary Pain Center) colleagues who have followed my work over the last 5 years.

All the patients who participated in my studies and made this research possible.

My family and friends for their patience.

Malene and Martin, my joy and pride.

Michael, my love and best friend.

QUESTIONNAIRES

Epworth Sleepiness Scale (ESS)

The ESS assesses the likelihood of the patient dozing off or falling asleep in eight daily situations using a score between 0 – 3. The maximum score is thus 24 with a score of 10 or more being taken to indicate significant levels of daytime sleepiness (13;38;39).

Brief Sexual Function Inventory (BSFI)

The BSFI is a 11 items measure, in which the first ten items cover functional aspects of male sexuality during the past thirty days: Sexual drive and level of sexual drive (two items), partial or full erection, capability to intercourse and difficulties in getting erection (three items), difficulty ejaculating and satisfaction with amount of semen (two items) and problem assessment concerning sexual drive, erection and ejaculation (three items). The last item covers overall sexual satisfaction and consists of one question. Higher scores represent indicating better function (16).

Female Sexual Function Index (FSFI)

The FSFI is a 19 item, multidimensional, self- report measure comprised of a full scale and six subscales (Desire, Lubrication, Arousal, Orgasm, Satisfaction and Pain) to measure sexual function. The measure was designed for clinical trials. FSFI has a score ranging from 2 to 36. Higher scores represent no sexual difficulties. Scores below the cut off ≤ 26.55 represent sexual difficulties (17;18).

Female Sexual Distress Scale (FSDS)

The FSDS is a 12-item self-report assessment questionnaire. It was developed to measure sexually related personal distress in women. The distress is scored on a scale from 0 to 6 for each item, with higher score indicating higher distress. Scores above the cut off ≥ 15 represent sexual distress (19).

Life satisfaction 11 (LiSat-11)

LiSat—11 is a 11 item self-reported assessment questionnaire from which we selected four questions concerning general satisfaction with life: Life as a Whole and three domains of closeness (Sexual Life, Partner Relationship, Family Life). Satisfaction was scored on a scale from 1-6, with higher scores indicating greater satisfaction. (14).

Demographic questionnaire

The questionnaire included items related to age, marital status, regular sexual partner, employment, education and use of medicine (Cardiovascular medication, Psychopharmaca and Antidiabetics).

REFERENCE LISTE

- (1) Basson R, Schultz WW. Sexual sequelae of general medical disorders. *Lancet* 2007 February 3;369(9559):409-24.
- (2) Christensen BS, Gronbaek M, Osler M, Pedersen BV, Graugaard C, Frisch M. Sexual dysfunctions and difficulties in denmark: prevalence and associated sociodemographic factors. *Arch Sex Behav* 2011 February;40(1):121-32.
- (3) Laumann EO, Nicolosi A, Glasser DB, Paik A, Gingell C, Moreira E, Wang T. Sexual problems among women and men aged 40-80 y: prevalence and correlates identified in the Global Study of Sexual Attitudes and Behaviors. *Int J Impot Res* 2005 January;17(1):39-57.
- (4) Montorsi F, Basson R, Adaikan G, Becher E, Clayton A, Giuliano F, Khoury S, Sharlip I. *Sexual medicine, Sexual Dysfunction in men and women.* 2010.
Ref Type: Edited Book
- (5) Hatzichristou D, Rosen RC, Derogatis LR, Low WY, Meuleman EJ, Sadovsky R, Symonds T. Recommendations for the clinical evaluation of men and women with sexual dysfunction. *J Sex Med* 2010 January;7(1 Pt 2):337-48.
- (6) Heiman JR, Long JS, Smith SN, Fisher WA, Sand MS, Rosen RC. Sexual satisfaction and relationship happiness in midlife and older couples in five countries. *Arch Sex Behav* 2011 August;40(4):741-53.
- (7) Oberg K, Fugl-Meyer AR, Fugl-Meyer KS. On categorization and quantification of women's sexual dysfunctions: an epidemiological approach. *Int J Impot Res* 2004 June;16(3):261-9.
- (8) Petersen CD, Giraldi A, Lundvall L, Kristensen E. Botulinum toxin type A-a novel treatment for provoked vestibulodynia? Results from a randomized, placebo controlled, double blinded study. *J Sex Med* 2009 September;6(9):2523-37.

- (9) Epstein LJ, Kristo D, Strollo PJ, Jr., Friedman N, Malhotra A, Patil SP, Ramar K, Rogers R, Schwab RJ, Weaver EM, Weinstein MD. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med* 2009 June 15;5(3):263-76.
- (10) Malhotra A, White DP. Obstructive sleep apnoea. *Lancet* 2002 July 20;360(9328):237-45.
- (11) Peker Y, Hedner J, Norum J, Kraiczi H, Carlson J. Increased incidence of cardiovascular disease in middle-aged men with obstructive sleep apnea: a 7-year follow-up. *Am J Respir Crit Care Med* 2002 July 15;166(2):159-65.
- (12) Yaggi HK, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V. Obstructive sleep apnea as a risk factor for stroke and death. *N Engl J Med* 2005 November 10;353(19):2034-41.
- (13) Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* 1991 December;14(6):540-5.
- (14) Fugl-Meyer AR, Melin R, Fugl-Meyer KS. Life satisfaction in 18- to 64-year-old Swedes: in relation to gender, age, partner and immigrant status. *J Rehabil Med* 2002 September;34(5):239-46.
- (15) O'Leary MP, Rhodes T, Girman CJ, Jacobson DJ, Roberts RO, Lieber MM, Jacobsen SJ. Distribution of the Brief Male Sexual Inventory in community men. *Int J Impot Res* 2003 June;15(3):185-91.
- (16) Mykletun A, Dahl AA, O'Leary MP, Fossa SD. Assessment of male sexual function by the Brief Sexual Function Inventory. *BJU Int* 2006 February;97(2):316-23.
- (17) Rosen R, Brown C, Heiman J, Leiblum S, Meston C, Shabsigh R, Ferguson D, D'Agostino R, Jr. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. *J Sex Marital Ther* 2000 April;26(2):191-208.
- (18) Wiegel M, Meston C, Rosen R. The female sexual function index (FSFI): cross-validation and development of clinical cutoff scores. *J Sex Marital Ther* 2005 January;31(1):1-20.
- (19) Derogatis LR, Rosen R, Leiblum S, Burnett A, Heiman J. The Female Sexual Distress Scale (FSDS): initial validation of a standardized scale for

assessment of sexually related personal distress in women. *J Sex Marital Ther* 2002 July;28(4):317-30.

- (20) Ronksley PE, Hemmelgarn BR, Heitman SJ, Hanly PJ, Faris PD, Quan H, Tsai WH. Obstructive sleep apnoea is associated with diabetes in sleepy subjects. *Thorax* 2009 October;64(10):834-9.
- (21) Schober AK, Neurath MF, Harsch IA. Prevalence of sleep apnoea in diabetic patients. *Clin Respir J* 2011 July;5(3):165-72.
- (22) Reishtein JL, Maislin G, Weaver TE. Outcome of CPAP treatment on intimate and sexual relationships in men with obstructive sleep apnea. *J Clin Sleep Med* 2010 June 15;6(3):221-6.
- (23) Cross MD, Mills NL, Al-Abri M, Riha R, Vennelle M, Mackay TW, Newby DE, Douglas NJ. Continuous positive airway pressure improves vascular function in obstructive sleep apnoea/hypopnoea syndrome: a randomised controlled trial. *Thorax* 2008 July;63(7):578-83.
- (24) Borges R, Temido P, Sousa L, Azinhais P, Conceicao P, Pereira B, Leao R, Retroz E, Brandao A, Cristo L, Sobral F. Metabolic syndrome and sexual (dys)function. *J Sex Med* 2009 November;6(11):2958-75.
- (25) Hasan A, Uzma N, Swamy TL, Shoba A, Kumar BS. Correlation of clinical profiles with obstructive sleep apnea and metabolic syndrome. *Sleep Breath* 2011 January 27.
- (26) Onem K, Erol B, Sanli O, Kadioglu P, Yalin AS, Canik U, Cuhadaroglu C, Kadioglu A. Is sexual dysfunction in women with obstructive sleep apnea-hypopnea syndrome associated with the severity of the disease? A pilot study. *J Sex Med* 2008 November;5(11):2600-9.
- (27) Koseoglu N, Koseoglu H, Itil O, Oztura I, Baklan B, Ikiz AO, Esen AA. Sexual function status in women with obstructive sleep apnea syndrome. *J Sex Med* 2007 September;4(5):1352-7.
- (28) Subramanian S, Bopparaju S, Desai A, Wiggins T, Rambaud C, Surani S. Sexual dysfunction in women with obstructive sleep apnea. *Sleep Breath* 2010 February;14(1):59-62.
- (29) Subramanian S, Guntupalli B, Murugan T, Bopparaju S, Chanamolu S, Casturi L, Surani S. Gender and ethnic differences in prevalence of self-reported insomnia among patients with obstructive sleep apnea. *Sleep Breath* 2011 December;15(4):711-5.

- (30) Giraldi A, Kristensen E. Sexual dysfunction in women with diabetes mellitus. *J Sex Res* 2010 March;47(2):199-211.
- (31) Kadioglu P, Yetkin DO, Sanli O, Yalin AS, Onem K, Kadioglu A. Obesity might not be a risk factor for female sexual dysfunction. *BJU Int* 2010 November;106(9):1357-61.
- (32) Yaylali GF, Tekekoglu S, Akin F. Sexual dysfunction in obese and overweight women. *Int J Impot Res* 2010 July;22(4):220-6.
- (33) Shifren JL, Monz BU, Russo PA, Segreti A, Johannes CB. Sexual problems and distress in United States women: prevalence and correlates. *Obstet Gynecol* 2008 November;112(5):970-8.
- (34) Basson R, Rees P, Wang R, Montejo AL, Incrocci L. Sexual function in chronic illness. *J Sex Med* 2010 January;7(1 Pt 2):374-88.
- (35) Johannes CB, Clayton AH, Odom DM, Rosen RC, Russo PA, Shifren JL, Monz BU. Distressing sexual problems in United States women revisited: prevalence after accounting for depression. *J Clin Psychiatry* 2009 December;70(12):1698-706.
- (36) Petersen M, Kristensen E, Berg S, Midgren B. Sexual function in male patients with obstructive sleep apnoea. *Clin Respir J* 2010 July;4(3):186-91.
- (37) Hartmann U, Philippsohn S, Heiser K, Ruffer-Hesse C. Low sexual desire in midlife and older women: personality factors, psychosocial development, present sexuality. *Menopause* 2004 November;11(6 Pt 2):726-40.
- (38) Goncalves MA, Guilleminault C, Ramos E, Palha A, Paiva T. Erectile dysfunction, obstructive sleep apnea syndrome and nasal CPAP treatment. *Sleep Med* 2005 July;6(4):333-9.
- (39) Weaver TE, Laizner AM, Evans LK, Maislin G, Chugh DK, Lyon K, Smith PL, Schwartz AR, Redline S, Pack AI, Dinges DF. An instrument to measure functional status outcomes for disorders of excessive sleepiness. *Sleep* 1997 October;20(10):835-43.
- (40) Pescatori ES, Giammusso B, Piubello G, Gentile V, Farina FP. Journey into the realm of requests for help presented to sexual medicine specialists: introduction male sexual distress. *J Sex Med* 2007 May;4(3):762-70.