

Dansk Neurologisk Selskabs  
**ÅRSMØDE**

fredag den 4. april - lørdag den 5. april 2008



**Munkebjerg**  
Munkebjergvej 125  
7100 Vejle



## SHARING your expertise



**Dysport, pulver til injektionsvæske, opløsning (clostridium botulinum type A toxin 500 enh.)**\*. Nedenstående produktinformation er uddrag af det godkendte produktresumé for Dysport, som kan rekvireres vederlagsfrit fra Institut Produkt Synthèse (IPSEN) AB. **Indikationer:** Blefarospasme hos voksne. Spasmodisk torticollis hos voksne. Persistentere svær primær aksillær hyperhidrose, der interfererer med daglige gøremål og som ikke responderer på topikale behandlingsmidler. **Dosering:**\* Alle de angivne enheder af botulinumtoxin gælder kun for Dysport og kan ikke overføres på andre botulinumtoxinpræparater. Blefarospasme: Til voksne og ældre anbefales 120 E pr. øje ved dobbeltsidig blefarospasme. Virkningen forventes at indtræde inden for 2 - 4 dage med maksimal effekt inden for 2 uger. I tilfælde af ensidig blefarospasme begrænses injektionerne til det angrebne øje. Spasmodisk torticollis: Til voksne og ældre normalvægtige uden tegn på lav muskelmasse i halsregionen er initialdosis 500 E givet som en delt dosis - injiceret i de 2 eller 3 mest aktive halsmuskler. Injektionerne bør gentages ca. hver 12. uge eller efter behov for at undgå symptomerne genopstår. Aksillær hyperhidrosis: Initialdosis til voksne og ældre er 100 E per armhule med intradermal injektion ti steder, 10 Enheder hvert sted. Der kan dog gives op til 200 E per armhule ved efterfølgende injektioner, hvis ønskes effekt ikke er opnået. Der må ikke behandles oftere end hver 12. uge, og der er tegn på kumulativ effekt ved gentagne doser. **Kontraindikation:** Dysport er kontraindiceret til patienter med kendt overfølsomhed over for det aktive stof eller over for et eller flere af hjælpestofferne. **Særlige advarsler og forsigtighedsregler:** Dysport bør administreres med forsigtighed til patienter med synke eller vejrtrækningsproblemer, da disse problemer kan forværes, hvis toxinet spredes til omkringliggende muskler. I sjældne tilfælde er aspiration forekommet. Aspiration er en risiko ved behandling af patienter med spasmodisk torticollis, som har en kronisk respiratorisk sygdom. Der er i meget sjældne tilfælde rapporteret dødsfald, i forbindelse med dysphagia, pneumopati og/eller hos patienter med signifikant asteni, efter behandling med botulinumtoksin A eller B. Patienter med lidelser, som resulterer i defekt neuromuskulær transmission eller vanskeligheder med at synke eller ånde, har større risiko for at opleve disse bivirkninger. Hos disse patienter må botulinumtoksin kun indgives under speciallistkontrol og kun hvis fordelene ved behandlingen opvejer risikoen. Patienter og deres plejere skal advares om nødvendigheden af øjeblikkelig medicinsk behandling, hvis patienten får problemer med at synke, tale eller trække vejret. Dysport skal anvendes med forsigtighed og under nøje overvågning til patienter med subklinisk og tidligere kraftig forringet neuromuskulær transmission (f.eks. Myasthenia Gravis). Der er noteret sjældne tilfælde af antistofdannelse mod botulinumtoxin hos patienter, der får Dysport. Dette præparat

indeholder en lille mængde humant albumin. Risikoen for overførsel af infektion kan ikke med sikkerhed udelukkes, idet der er anvendt humant blod eller blodprodukter. **Interaktioner:** Lægemidler, som påvirker den neuromuskulære transmission f.eks. aminoglykosider bør anvendes med forsigtighed. **Bivirkninger:**\* Følgende bivirkninger er rapporteret hos patienter behandlet med Dysport. Hyppighederne er defineret således: Meget almindelig (>1/10), almindelig (>1/100 og <1/10), ikke almindelig (>1/1000 og <1/100), sjældent (>1/10.000 og <1/1000). Alle bivirkningerne er milde og forbigående. Generelle (blefarospasme, hemifaciale spasmer, torticollis): Almindelig: generel svaghed, træthed, influenzalignende symptomer, smerte/blåt mærke på injektionsstedet. Ikke almindeligt: kløe. Sjældent: neuralgisk amyotrofi-, hududslæt. Patienter behandlet for spasmodisk torticollis har rapporteret følgende bivirkninger: Meget almindelig: dysfagi (dosis-afhængig og forekommer hyppigt efter injektion i sternomatoid-musklen. En mild diæt kan være nødvendig indtil symptomerne er gået over). Almindelig: dysfoni, svaghed af nakkemuskler. Ikke almindelig: hovedpine, dobbeltsyn, sløret syn, mundtørhed. Sjældent: respiratoriske sygdomme. Patienter behandlet for blefarospasme og hemifaciale spasmer: Meget almindelig: ptosis. Almindelig: svaghed af ansigtsmuskler, dobbeltsyn, tørre øjne, tåreflåd, øjenlåg ødem. Ikke almindelig: lammelse af ansigtsnerv, ophthalmoplegi. Sjældent: entropion. Bivirkningerne kan skyldes midlertidig lammelse af andre nærvedliggende muskelgrupper på grund af dybe eller forkert placerede Dysport injektioner. Bivirkningsprofilen efter markedsføringen reflekterer produktets farmakologi og profil set i de kliniske studier. Aksillær hyperhidrosis: Almindelig: dyspnø, kompensatorisk hyperhidrosis, smerte i skulder, øvre arm og nakke, myalgi i skulder og læg. Ikke almindelig: Svimmelhed, hovedpine og paræstesi, ufrivillige muskeltkræmper i øjenlåg, rødmen, næseblod, øget svedafsondring på andre hudpartier. Sjældent: allergiske reaktioner, såsom hududslæt. Der er i meget sjældne tilfælde rapporteret om bivirkninger, som er et resultat af distribution af toksinets virkning til steder fjernt fra administrationsstedet (usædvanlig stor muskelsvaghed, dysphagia, aspirationspneumonia, som kan være fatal). De fleste bivirkninger er milde og forbigående. **Registreringsindehaver:** Institut Produkt Synthèse (IPSEN) AB, Fåregatan 33, SE-164 51 Kista, Sverige. MT nr.: 14586. **Udlevering:** Må kun udleveres til sygehuse, eller efter ordination af speciallæger i oftalmologi, neurologi, plastikkirurgi og dermatovenerologi. **Lægemiddelform:** Pulver til injektionsvæske, opløsning i hætteglas á 500 enheder Clostridium botulinum type A toxin. **Priser og pakninger:** 2 x 500 IE 5410.45 kr. (9. januar 2007). For dagaktuelle priser se venligst [www.medicinpriser.dk](http://www.medicinpriser.dk). **Tilskudsregler:** Ikke tilskudsberettiget, 27. august 2007

**Dysport®**  
Botulinum Toxin Type A

## **Årsmødet er sponsoreret af**

Merck Sharp & Dohme

UCB Nordic A/S

Bayer Schering Pharma

## **Udstillere på årsmødet**

UCB Nordic A/S

Medtronic Danmark A/S

Allergan Inc.

Ipsen Nordic



# Små ting betyder så meget

**BOTOX®**  
Botulinumtoksin type A  
Oprenset neurotoksinkompleks

1. Brashear A et al. Intramuscular injection of botulinum toxin for the treatment of wrist and finger spasticity after a stroke. *N Engl J Med.* 2002;347(6):395-400.

## BOTOX® Forkortet produktinformation

Præsentation: Hætteglas med 100 Allergan-enheder (E) Botulinumtoksin type A, fra *Clostridium botulinum*.

**Indikationer:** Botox® er indiceret til behandling af: Blefarospasme, halvsidig facialispasme og ledsagende fokale dystonier. Cervikal dystoni (spastisk torticollis). Fokal spasticitet: i forbindelse med dynamisk spidsfødsdeformitet på grund af spasticitet hos oppegående patienter med infantil cerebral parese i alderen fra 2 år og opæfter; af hånd og hånd hos voksne patienter efter slagtilfælde. Persisterende, svar primær hyperhidrosis i aksillerne, der hæmmer dagligdags aktiviteter, og som er resistent over for lokalbehandling.

**Dosering og indgivelsesmåde:** For fuldstændige oplysninger henvises til Produktresuméet. Rekonstitueres med sterilt ukonserveret almindeligt saltvand (0,9 % natriumchlorid til injektionsvæske). Botulinumtoksin-enhederne kan ikke udskiftes fra et produkt til et andet. **Blefarospasme:** Injicér med en kanyle på 27–30 gauge. Initialt injiceres der 1,25–2,5 E medialt og lateralt i øvre øjenlægs orbicularis oculi og lateralt i nedre øjenlægs orbicularis oculi. Derefter kan dosen øges op til to gange. Initialdosen må ikke overstige 25 E pr. øje. Den totale dosering må ikke overstige 100 E hver 12. uge. **Halvsidig facialispasme:** Behandling som ved ensidig blefarospasme (se herover). Injicér andre berørte facialmuskler efter behov. **Cervikal dystoni:** Injicér med en kanyle af passende størrelse (i reglen 25–30 gauge). Tilpas doseringen til den enkelte patient baseret på muskelmassen og graden af hypertrofi eller atrofi. M. sternocleidomastoideus må ikke injiceres bilateralt. Der må ikke injiceres mere end 200 E i alt ved første behandlingsserie. En totaldosis på 300 E må ikke overskrides ved nogen enkelt seance. **Infantil cerebral parese:** Injicér med en kanyle på 23–26 gauge som en delt dosis i form af enkeltinjektioner i det mediale og det laterale muskelhoved af den afficerede gastrocnemiusmuskulatur. Ved hemiplegi er den anbefalede totaldosis 4 E/kg; ved diplegi 6 E/kg fordelt mellem de afficerede ekstremiteter. Den totale dosis bør ikke overstige 200 E. Dosis må ikke gentages hyppigere end hver 3. måned. **Fokal spasticitet af overekstremitet efter slagtilfælde:** Injicér med en kanyle på 25, 27 eller 30 gauge til superficiele muskler og en længere kanyle til dybere liggende muskulatur. Flere injektionssteder kan give Botox® mulighed for at få mere ensartet kontakt med innervationsområderne i musklen og er især nyttigt ved større muskler. Tilpas dosis og antal steder baseret på de involverede musklers størrelse, antal og lokalisering, sværhedsgraden af spasticitet, tilstedeværelse af lokal muskelsvaghed og patientens respons på tidligere behandling. Der må ikke gives re-injektioner før efter 12 uger. **Primær hyperhidrosis i aksillerne:** Injicér med en kanyle på 30 gauge. Injicér 50 E intrakutan ligeligt fordelt på flere steder med ca. 1–2 cm afstand i hver aksill. Der kan gives fornyet injektion, når den kliniske effekt af en forudgående injektion aftager. Injektionerne må ikke gentages hyppigere end hver 16. uge.

**Kontraindikationer:** Botox® er kontraindiceret: Hos personer med kendt overfølsomhed over for botulinumtoksin type A eller et eller flere af hjælpestofferne. I tilfælde af infektion ved det påtænkte injektionssted. **Advarsler/forsigtighedsregler:** Den relevante anatomi og enhver ændring af anatomi på grund af forudgående kirurgiske indgreb skal være kendt for indgivelse. Adrenalin og andre anti-anginalmidler skal være til rådighed. Der er rapporteret bivirkninger, der skyldes udbredelse af toksinet fjæret fra injektionsstedet, der nogle gange førte til dødsfald. Udvis største forsigtighed hos patienter med underliggende neurologiske forstyrrelser samt anamnese for dysfagi og aspiration. Patienter eller plejepersonale skal søge omgående medicinsk behandling, hvis der opstår synke-, tale- eller vejrtrækningsbesvær. Der kan forekomme kliniske variationer ved gentagen anvendelse. For hyppig eller usædvanlig stor dosering kan resultere i antistofdannelse og resistens over for behandlingen. Tidligere stillesiddende patienter skal gradvist genoptage deres aktiviteter. Der skal udvises forsigtighed ved inflammation ved injektionsstedet/-stederne eller ved udtalt slaphed/atrofi i målområdet. Der skal udvises forsigtighed ved anvendelse til behandling af patienter med amyotrofisk lateralsklerose eller motorisk neuropati. Anvendes med største forsigtighed og under nøje overvågning til patienter med defekt neuromuskulær transmission (myasthenia gravis, eller Eaton Lambert-syndrom). Indeholder humant albumin. Der kan opstå procedurerelateret skade. **Blefarospasme:** Nedsat blinkerefleks efter injektion i m. orbicularis kan resultere i patologiske forhold i cornea. Der skal foretages omhyggelig testning af corneas følsomhed i øjne, hvor der tidligere er udført operation, undlades injektion i det nedre øjenlægsområde for at undgå ekotropion og foretages energisk behandling af enhver epiteldefekt. Der kan forekomme ekkymose. Der skal udvises forsigtighed ved behandling af patienter med risiko for vinkelbløkkglaukom. **Cervikal dystoni:** Der kan opstå synkebesvær, som kan være meget mildt, men også være svært. Begrænsning af dosis i m. sternocleidomastoideus til mindre end 100 E kan eventuelt reducere forekomsten af synkebesvær. **Fokal spasticitet i forbindelse med infantil cerebral parese samt hos voksne patienter efter slagtilfælde:** Ikke tænkt som erstatning for de sædvanlige standardbehandlingsregimer. Er sandsynligvis ikke virksomt til bedring af bevægelsesområdet af et led, der er afficeret af en fikseret kontraktur. **Primær hyperhidrosis i aksillerne:** Overvej sekundære årsager til hyperhidrosis for at undgå symptomatisk behandling uden diagnosticering og/eller behandling af tilgrundsliggende sygdom.

**Interaktioner:** Effekten kan potenseres af aminoglykosid-antibiotika eller spectinomycin, eller andre medicinske produkter som interfererer med neuromuskulær transmission f.eks. muskelrelaxantia af tubocurarin-typen. Virkningen af administration af forskellige serotyper af botulinum neurotoksin samtidig eller inden for nogle måneders forløb kendes ikke. Voldsom neuromuskulær svækkelse kan forstærkes ved administration af et andet botulinumtoksin, for virkningen af det tidligere administrerede botulinumtoksin har fortaget sig.

**Bivirkninger:** *Generelt:* I reglen optræder uønskede hændelser inden for de første få dage efter injektionen, og de er kortvarige. Lokal muskelslaphed repræsenterer den forventede farmakologiske virkning. Injektionen kan være forbundet med lokal smerte, ømhed og/eller blå mærker. Der er rapporteret feber og influenzasyndrom. *Hyppighed efter indikation:* Frekvensen defineres som følger: Meget almindelig (> 1/10); almindelig (> 1/100, < 1/10.000); ikke almindelig (> 1/1.000, < 1/100); sjælden (> 1/10.000, < 1/1.000); meget sjælden (< 1/10.000). **Blefarospasme/halvsidig facialispasme:** Meget almindelig: Ptose af øjenlåg. Almindelig: Punktformig keratitis, lagophthalmus, tørre øjne, lysskyhed og øget tåreflåd. Irritation og ansigtsødem. Ikke almindelig: Svimmelhed, facialispasme og Bells parese. Keratitis, ekotropion, diplopi, entropion, synsforstyrrelse og uskarpt syn. Udslet, dermatitis. Træthed. Sjælden: Øjenlægsødem. Meget sjælden: Cornealceration. **Cervikal dystoni:** Meget almindelig: Dysphagi. Muskelsvækkelse. Smerter. Almindelig: Rhinitis og øvre luftvejsinfektion. Svimmelhed, hypertoni, hypoæstesi, somnolens og hovedpine. Mundtørhed og kvalme. Stivhed i skeletmuskulaturen og ømhed. Asteni, influenza lignende sygdom og utilpashed. Ikke almindelig: Diplopi og ptose af øjenlåg. Dyspnø og dysfoni. Pyreksi. **Infantil cerebral parese:** Meget almindelig: Virusinfektion og øreinfektion. Almindelig: Somnolens og paræstesi. Udslet. Myalgi og muskelsvækkelse. Urininkontinens. Gangforstyrrelser og utilpashed. **Fokal spasticitet af overekstremitet i forbindelse med slagtilfælde:** Almindelig: Hypertoni. Ekkymose og purpura. Smerter i ekstremitet og muskelsvækkelse. Blødning ved injektionsstedet og irritation ved injektionsstedet. Ikke almindelig: Depression og insomni. Hypoæstesi, hovedpine, paræstesi, manglende koordination og amnesi. Vertigo. Ortostatisk hypotension. Kvalme og oral paræstesi. Dermatitis, pruritus og udslet. Artralgi og bursitis. Asteni, smerter, overfølsomhed ved injektionsstedet, utilpashed og perifert ødem. (Nogle af de ualmindelige hændelser kan være sygdomsrelaterede). **Primær hyperhidrosis i aksillerne:** Almindelig: Hovedpine. Hedetur. Kvalme. Hyperhidrosis (ikke-aksillære svedudbrud). Pruritus. Reaktionen ved injektionsstedet og smerter. Ikke almindelig: Muskelsvækkelse, myalgi, arthropati og smerter i ekstremitet. Asteni, ødem ved injektionsstedet og smerter ved injektionsstedet.

**Yderligere information:** Der foreligger meget sjældne rapporter om bivirkninger relateret til spredning af toksinet fjæret fra administrationsstedet (voldsom muskelsvækkelse, dysphagi, aspiration, som iblandt førte til udvikling af aspirationspneumoni, i nogle tilfælde med dødeligt udfald). Følgende andre bivirkninger er rapporteret siden produktet kom på markedet: dysartri, abdominalsmarter; uskarpt syn, pyreksi, fokal facialispasme, hypoæstesi, utilpashed, myalgi, pruritus, hyperhidrosis, diaré, anoreksi, hypoacusis, tinnitus, radikulopati, synkope, myasthenia gravis, erythema multiforme, psoriasisform dermatitis, opkastning og plexopathia brachialis. Der har også været sjældne rapporter om uønskede hændelser, der involverede det kardiovaskulære system omfattende arytmier og myokardieinfarkt, nogle med fatal udgang. Der foreligger sjældne rapporter om alvorlige og/eller umiddelbare overfølsomhedsreaktioner, som omfatter anafylaksi, serumsygdom, urticaria, ødem i blødt væv og dyspnø. Nogle af disse reaktioner rapporteres efter brug af Botox® enten alene eller sammen med andre stoffer, der vides at kunne udløse lignende reaktioner. Et tilfælde af perifer neuropati er blevet rapporteret. Debuterende eller recidiverende krampeanfald er forekommet – typisk hos patienter, som er disponeret for denne type hændelser. Vinkelbløkkglaukom er meget sjældent blevet rapporteret. **Primær aksillær hyperhidrosis:** Forøget ikke-aksillær sveden blev rapporteret hos 4,5 % af patienterne inden for 1 måned efter injektion, og den viste intet mønster med hensyn til påvirkede anatomiske steder. Der sås resolution hos ca. 30 % af patienterne inden for fire måneder. Desuden er svaghed af armene rapporteret som ikke almindelig (0,7 %). Sjældne rapporter om epileptiske anfald eller kramper. Smerter og/eller ængstelse relateret til injektionsnålen kan medføre vasovagale reaktioner.

**Pakningsstørrelser og priser:** Botox® 100 Allergan-enheder/hætteglas: 2709,60 DKK. Dato: Juli 2007. **Endvidere henvises til dagsaktuel pris på [www.medicinpriser.dk](http://www.medicinpriser.dk).** Udløbering NBS. **Indehaver af markedsføringstilladelsen:** Allergan Pharmaceuticals Ireland, Castlebar Road, Westport, County Mayo, Irland. **Yderligere oplysninger kan fås hos:** Allergan Norden AB, Johanneslundsvägen 3-5, S-194 81 Upplands Väsby, Sverige. **Baseret på produktresumé dateret:** Juni 2007.

**Produktinformationen er forkortet i forhold til det af Lægemiddelstyrelsens godkendte produktresumé. Produktresuméet kan vederlagsfrit rekvireres fra Allergan.**

# Indholdsfortegnelse

- **Program/tidsplan til DNS' årsmøde**
- **Mogens Fog Foredragskonkurrence 2008**
- **Abstracts til Mogens Fog konkurrencen**
  - Escitalopram in painful polyneuropathy
  - The cholinomimetic agent carbachol induces headache in healthy subjects
  - Voxelwise brain analysis in optic neuritis
  - Length dependent weakness and electrophysiological signs of secondary axonal loss in chronic inflammatory demyelinating polyradiculoneuropathy
  - NO induces axonal degeneration of active peripheral mouse nerves by interfering with energy supply
  - Effect of methylprednisolone on neutralizing antibodies after discontinuation of interferon-beta treatment
  - Calcitonin gene-related peptide is not causative for the familial hemiplegic migraine phenotype
  - Body mass index positively correlated with frontal 5-HT<sub>2A</sub> receptor binding in humans
  - Binge Drinking during Pregnancy and Risk of Seizures in Childhood
  - Abnormal hemodynamic response to tilt table test in patients with complex regional pain syndrome
- **Poster Session**
- **Abstracts til Posters der ikke er med i Mogens Fog Konkurrencen**
  - Idiopathic intracranial hypertension and venous thrombophilia
    - A case-control study of risk factors
  - Long term risk of epilepsy after thumatic brain injury in children and young adults – a population-based cohort study
  - Central pain after experimental spinal cord injury: histological characterisation
  - Neck artery dissection and symptomatic headache mimicking primary headache types
  - Separation of pain and reflex responses in an animal model of spinal cord injury
  - LRRK2 G2019S point mutation screening of Danish subjects with Parkinson's Disease and Atypical Parkinsonian Syndromes
  - A postal survey on post-stroke pain

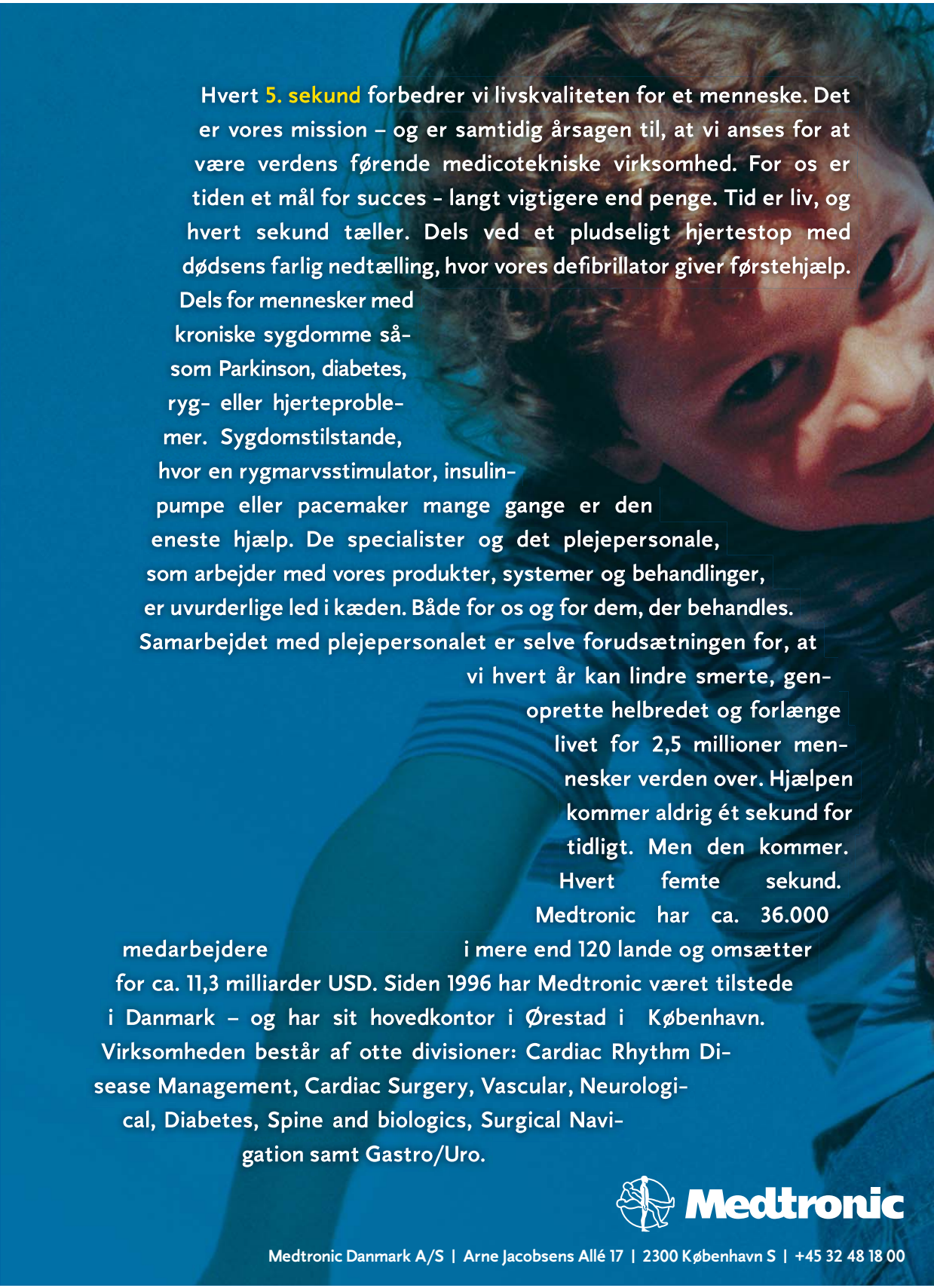
# Program/tidsplan til DNS' årsmøde

## Fredag den 4. april 2008

- 10.00-10.30     **Kaffe + udstilling**
- 10.30-10.35     **Velkomst**  
Formand Olaf B. Paulson
- 10.35-11.20     **Session I – Professorforelæsning  
– Postgraduat neurologisk uddannelse**  
Professor, overlæge, dr.med. Flemming W. Bach,  
Neurologisk afd., Aalborg Sygehus
- 11.20-11.25     Strække ben pause
- 11.25-13.10     **Session II – Mogens Fog Foredragskonkurrence**
- 13.10-14.00     **Frokost + Udstilling**
- 14.00-14.45     **Session III – Årets tre cases fra den neurologiske raritets-  
kasse – interaktiv session med fremvisning af patienter  
på DVD og kommentarer fra eksperter.**  
Sessionen i 2008 tilrettelægges af Roskilde
- 14.45-14.55     Strække ben pause
- 14.55-15.40     **Session IV – Diagnostik og behandling  
af tremorpatienten**  
Overlæge Tove Henriksen, Neurologisk afd. N,  
Bispebjerg Hospital
- 15.40-16.30     **Postersession, kaffe + udstilling**
- 16.30-18.00     **Session V – Neurobowl**  
Overlæge, dr.med. Klaus Hansen, Neurologisk Klinik,  
Rigshospitalet
- 18.00-19.00     Pause
- 19.00-02.00     **Festmiddag**  
Årets uddannelsesprismodtager

## Lørdag den 5. april 2008

- 09.00-10.00     **Session VI – Patientklager – hvordan håndteres en klagesag**  
Overlæge Kurt Lühdorf, der i en lang årrække har været sagkyndig i Patientklagenævnet, vil desuden som udgangspunkt i 50 konsekutive klager gennemgå klage typer samt hvordan nogle af disse evt. kan forebygges
- 10.00-10.15     Strække ben pause
- 10.15-11.00     **Session VII – Hot topic: Nyt behandlingsprincip ved genetisk sygdom – eksemplificeret ved model for protein silencing ved familiær-ALS (SOD1-mutationer)**  
Overlæge, dr.med. Peter Munch Andersen, Umeå
- 11.00-11.30     **Kaffe + udstilling**
- 11.20-12.30     **Session VIII – Hvad sker der med pt. på subspecial afdelingen – behandlings- og forskningsmæssige aspekter**  
*Status for amyloid-scanning ved degenerative sygdomme*  
Overlæge, dr.med. Steen Hasselbalch, Hukommelseskliniken, Nationalt Videnscenter for Demens, Righospitalet  
*Status for vaccinationsbehandling ved Alzheimers sygdom*  
Overlæge, Ph.d. Peter Johannsen, Hukommelseskliniken, Nationalt Videnscenter for Demens, Righospitalet
- Årets uddannelsesprismodtager**  
– præsentation af afdelingens/personens/kursistens uddannelses tiltag (efter forslag fra yngre neurologer)
- 12.30             **Afskeds sandwich eller let anretning**



Hvert **5. sekund** forbedrer vi livskvaliteten for et menneske. Det er vores mission – og er samtidig årsagen til, at vi anses for at være verdens førende medicotekniske virksomhed. For os er tiden et mål for succes – langt vigtigere end penge. Tid er liv, og hvert sekund tæller. Dels ved et pludseligt hjertestop med dødsens farlig nedtælling, hvor vores defibrillator giver førstehjælp. Dels for mennesker med kroniske sygdomme såsom Parkinson, diabetes, ryg- eller hjerte problemer. Sygdomstilstande, hvor en rygmarvsstimulator, insulinpumpe eller pacemaker mange gange er den eneste hjælp. De specialister og det plejepersonale, som arbejder med vores produkter, systemer og behandlinger, er uvurderlige led i kæden. Både for os og for dem, der behandles. Samarbejdet med plejepersonalet er selve forudsætningen for, at vi hvert år kan lindre smerte, genoprette helbredet og forlænge livet for 2,5 millioner mennesker verden over. Hjælpen kommer aldrig ét sekund for tidligt. Men den kommer. Hvert femte sekund. Medtronic har ca. 36.000

medarbejdere i mere end 120 lande og omsætter for ca. 11,3 milliarder USD. Siden 1996 har Medtronic været tilstede i Danmark – og har sit hovedkontor i Ørestad i København. Virksomheden består af otte divisioner: Cardiac Rhythm Disease Management, Cardiac Surgery, Vascular, Neurological, Diabetes, Spine and biologics, Surgical Navigation samt Gastro/Uro.



# Mogens Fog Foredragskonkurrence 2008

Chairman: Professor, overlæge, dr.med. Per Soelberg Sørensen

- 1. Escitalopram in painful polyneuropathy**  
Marit Otto, Flemming W. Bach, Troels S. Jensen, Kim Brøsen, Søren H. Sindrup
- 2. The cholinomimetic agent carbachol induces headache in healthy subjects**  
Henrik Schytz, Troels Wienecke, Peter Oturai, Jes Olesen, Messoud Ashina
- 3. Voxelwise brain analysis in optic neuritis**  
Kirsten Korsholm, Kristoffer H. Madsen, Jette L. Frederiksen, James B. Rowe, Torben E. Lund
- 4. Length dependent weakness and electrophysiological signs of secondary axonal loss in chronic inflammatory demyelinating polyradiculoneuropathy**  
Thomas Harbo, Henning Andersen, Johannes Jakobsen
- 5. NO induces axonal degeneration of active peripheral mouse nerves by interfering with energy supply**  
Susana Alvarez, Mihai Moldovan, Christian Krarup
- 6. Effect of methylprednisolone on neutralizing antibodies after discontinuation of interferon-beta treatment**  
D Hesse, JL Frederiksen, N Koch-Henriksen, K Schreiber, E Stenager, A Heltberg, M Ravnborg, K Bendtzen, F Sellebjerg, PS Sørensen
- 7. Calcitonin gene-related peptide is not causative for the familial hemiplegic migraine phenotype**  
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- 8. Body mass index positively correlated with frontal 5-HT<sub>2A</sub> receptor binding in humans**  
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- 9. Binge Drinking during Pregnancy and Risk of Seizures in Childhood**  
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- 10. Abnormal hemodynamic response to tilt table test in patients with complex regional pain syndrome**  
Astrid J Terkelsen, Henning Mølgaard, John Hansen, Nanna B. Finnerup, Troels S Jensen

## Escitalopram in painful polyneuropathy: a randomized, controlled trial

Marit Otto<sup>1</sup>, Flemming W. Bach<sup>2</sup>, Troels S. Jensen<sup>3</sup>, Kim Brøsen<sup>4</sup>, Søren H. Sindrup<sup>1</sup>

### Introduction

Serotonin (5-HT) is involved in pain modulation via descending pathways in the central nervous system. Escitalopram is a selective serotonin reuptake inhibitor (SSRI). The aim of this study was to test if escitalopram would relieve pain in polyneuropathy.

### Methods

The study design was randomized, double-blind, placebo-controlled and cross-over. The daily dose of escitalopram was 20 mg once daily. During the two treatment periods of 5 weeks duration, patients rated pain relief (primary outcome variable) on a 6 point ordered nominal scale. Secondary outcome measures comprised total pain and different pain symptoms. Changes in health-related quality of life and depression were measured with the SF-36 and the Major Depression Inventory (MDI).

### Results

Forty-one patients were included in the data analysis. Pain relief was better during treatment with escitalopram compared to placebo ( $p=0.001$ ). Total pain and different pain symptoms were lower during escitalopram ( $p=0.001$  to  $0.024$ ). The Numbers needed to treat (NNT) to obtain one patient with moderate or better pain relief was 6.8. Health-related quality of life and depressive symptoms were unaltered during the study ( $p=0.086$  to  $1.0$ ). Five patients (10.4%) discontinued the study because of adverse effects during escitalopram.

### Conclusion

This study found a pain relieving effect of escitalopram in patients with painful polyneuropathy.

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- 1) Department of Neurology, Odense University Hospital, University of Southern Denmark,
  - 2) Department of Neurology, Aalborg Sygehus, Aarhus University Hospital
  - 3) Danish Pain Research Center, Aarhus University Hospital, University of Aarhus
  - 4) Institute of Public Health, Department of Clinical Pharmacology, University of Southern Denmark

# The cholinomimetic agent carbachol induces headache in healthy subjects

Henrik Schytz<sup>1</sup>, Troels Wienecke<sup>1</sup>, Peter Oturai<sup>2</sup>, Jes Olesen<sup>1</sup>,  
Messoud Ashina<sup>1</sup>

## Background

Head pain is generated by activation and sensitization of perivascular sensory afferent fibers. The parasympathic nervous system is believed to contribute to the sensitization of these fibers and thereby generation of headache.

## Hypothesis

Infusion of the cholinomimetic agent carbachol can induce headache and vasodilatation of cephalic vessels.

Method: We randomly allocated 12 healthy subjects to receive 3 µg/kg carbachol or placebo intravenously in a randomized, double blind cross over study. Headache was scored on a verbal rating scale from 0-10. Velocity in the middle cerebral artery ( $V_{MCA}$ ) and diameter of the superficial temporal artery (STA) were recorded.

## Results

During and after carbachol infusion 7 subjects reported headache on carbachol compared to 2 on placebo. Compared to placebo, carbachol infusion caused a significant drop in  $V_{MCA}$  ( $P=0.003$ ) and increase in the STA diameter ( $P=0.006$ ). Additional *in vitro* experiments on human cephalic arteries showed, that relaxation induced by acetylcholine is dependent on intact endothelium and nitric oxide production.

## Conclusion

A cholinomimetic agent can induce headache and dilatation of cephalic arteries. This study shows that an exogenously agent, which induce dilatation by production of endothelial NO, may induce headache.

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1) Danish Headache Center and Departments of Neurology

2) Clinical Physiology and Nuclear Medicine, Glostrup Hospital, University of Copenhagen, Glostrup, Denmark.

## Voxelwise brain analysis in optic neuritis

Kirsten Korsholm<sup>1</sup>, Kristoffer H. Madsen<sup>1,2</sup>, Jette L. Frederiksen<sup>3</sup>,  
James B. Rowe<sup>1,4</sup>, Torben E. Lund<sup>1,5</sup>

### Introduction

Optic neuritis (ON) is an optic neuropathy characterised by retrobulbar pain and transient visual impairment. Within weeks or months after onset of ON a spontaneous recovery of visual function usually occurs, however, the mechanisms behind the recovery are not clear. The aim of this study was to assess if activation occurs outside visual areas during recovery indicative of cortical adaptive changes as reported by two previous studies (*Werring et al. 2000; Toosy et al. 2002*).

### Methods

Visual activation was studied longitudinally in 19 patients with ON using functional magnetic resonance imaging (fMRI) and autoperimetry. A longitudinal voxelbased analysis was performed to study whole brain activation patterns during and after recovery from ON.

### Results

With the voxelwise analysis of whole brain activation it was demonstrated that the changes in visual activation during recovery are located to the visual cortex and the LGN. No changes in activation during or after recovery were found outside visual areas.

### Conclusion

No evidence of cortical adaptive changes was found, and it is most likely that recovery of vision in our population of ON patients is due to resolution of inflammation and oedema during the first months.

### References

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1) Danish Research Centre for Magnetic Resonance, Copenhagen University Hospital, Hvidovre, Denmark  
2) Informatics and Mathematical Modelling, Technical University of Denmark, Lyngby, Denmark,  
3) Department of Neurology, Copenhagen University Hospital, Glostrup, Denmark.  
4) Department of Clinical Neurosciences, Cambridge University, England.  
5) Center for Functionally Integrative Neuroscience, Aarhus University Hospital, Aarhus, Denmark.

## **Length Dependent Weakness and Electrophysiological signs of Secondary Axonal Loss in Chronic Inflammatory Demyelinating Polyradiculoneurpathy**

*Thomas Harbo, Henning Andersen, and Johannes Jakobsen  
Department of Neurology, Aarhus University Hospital*

In chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) the pathophysiology underlying permanent muscle weakness and sensory loss was studied in 22 stabilized long-term CIDP patients clinically characterized using isokinetic dynamometry, quantitative sensory testing and neuropathy scores. Conduction velocity (CV), distal latency (DLAT), minimal F-wave latency (FLAT), compound muscle action potential (CMAP), and amplitude decay between distal and proximal stimulation sites were determined in the median, ulnar, peroneal, and tibial motor nerves and sensory CV and nerve action potentials in the median and sural nerves. In CIDP amplitude of CMAP and the DLAT were related to quantitative muscle strength, whereas CV, FLAT, amplitude decay and dispersion were not consistently related to strength. Furthermore, CMAP and muscle strength were significantly more reduced distally than proximally. In conclusion, the electrophysiological signs of axonal loss and the associated length dependent muscle weakness suggest secondary axonal loss in addition to primary demyelination in CIDP.

## **NO induces axonal degeneration of active peripheral mouse nerves by interfering with energy supply**

*Susana Alvarez<sup>1</sup>; Mihai Moldovan<sup>1</sup>; Christian Krarup<sup>1,2</sup>*

Exposure of axons to the free radical Nitric Oxide (NO) triggers acute conduction block and if exposure is prolonged it may cause axonal degeneration. It was hypothesized that the effect of NO may be due to energy restriction by inhibition of mitochondrial respiration. We investigated the *in vivo* effect of NO exposure on active peripheral mouse nerves and compared this with exposure to the mitochondrial uncoupler 2, 4- dinitrophenol (DNP). The right tibial nerve was stimulated at ankle. CMAPs were recorded from plantar muscles. Corresponding CNAPs were recorded from the sciatic nerve. The sciatic nerve was immersed in either phosphate buffered saline (PBS), 10 mM (Z)-1-[2-(2-Aminoethyl)-N-(2-ammonioethyl)amino]diazene-1-ium-1,2-diolate (DETA NONOate), or up to 1 mM DNP. Following 3 hours of 200 Hz stimulation, the nerves were washed in PBS for 1 hour, the surgical wounds were closed and the mice were left to recover. After 24 hours, complete CMAP and CNAP recovery was ascertained in the nerves exposed to PBS. Acute exposure to NO or DNP had the same effects on axons: (i) a transient conduction failure and (ii) Wallerian degeneration of some axons confirmed at morphological studies. These data support the hypothesis that the neurotoxic effect of NO may be caused by energy restriction.

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1) Neurophysiology (INF), The PANUM Institute, Copenhagen  
2) Clinical Neurophysiology, Rigshospitalet, Copenhagen

## Effect of methylprednisolone on neutralizing antibodies after discontinuation of interferon-beta treatment

*Hesse D, Frederiksen JL, Koch-Henriksen N, Schreiber K, Stenager E, Heltberg A, Ravnborg M, Bendtzen K, Sellebjerg F, Sorensen PS*

Interferon-beta (IFN $\beta$ ) is first-line treatment in relapsing-remitting multiple sclerosis. However neutralizing antibodies (NAb), appearing in a variable proportion of patients, reduce IFN $\beta$  bioactivity and therapeutic efficacy. Initial combination therapy with methylprednisolone (MP) reduces the frequency of NAb+ patients.

We hypothesized that MP treatment in patients already NAb+ could affect NAb status and bioactivity after cessation of IFN $\beta$ .

In an open label trial, we compared monthly high-dose pulsed MP treatment for 6 months (n=38) to a control group (n=35), consisting of patients switching to glatiramer acetate or stopping any treatment. All patients were NAb+ with unmeasurable bioactivity. NAb levels were measured using a cytopathic effect assay and expressed as neutralizing capacity (NC), i.e. the neutralized percentage of IFN $\beta$  added to the sample. Bioavailability was expressed as in vivo MxA mRNA induction in whole blood using real time PCR.

At study end, median NAb NC was 92% in both groups. Eight patients (21%) in the MP group and four patients (11%) in the control group had regained an in vivo MxA response ( $p = 0.35$ , Fishers Exact Test).

In conclusion monthly pulsed MP treatment in NAb+ patients had no effect on NAb status or IFN $\beta$  bioactivity compared to a control group.

## Calcitonin gene-related peptide is not causative for the familial hemiplegic migraine phenotype

Jakob Møller Hansen<sup>1</sup>, Lise Lykke Thomsen<sup>2</sup>, Jes Olesen<sup>1</sup>, Messoud Ashina<sup>1</sup>

### Background and aims

Familial hemiplegic migraine (FHM) is a dominantly inherited subtype of migraine with aura and transient hemiplegia associated with several gene mutations. The onset of FHM is typically between 10-18 years of age, and is thus often diagnosed by pediatricians.

FHM share many phenotypical similarities with common types of migraine, indicating common neurobiological pathways. The neuropeptide calcitonin gene-related peptide (CGRP) plays a crucial role in migraine pathophysiology and CGRP-receptor antagonism has documented efficacy in the treatment of migraine attacks. CGRP is a migraine trigger because infusion of CGRP causes migraine attacks. The mechanisms underlying the migraine inducing effects of CGRP are still not known in detail, but the phenotype might be linked to the FHM mutations. Clarifying the functional consequences of FHM mutations by examining the sensitivity to known migraine triggers such as CGRP is a logical step in a bottom-up approach to understand the FHM phenotype. We therefore, tested the hypothesis that genotyped FHM patients show a similar hypersensitivity to activation of the CGRP-cAMP pathway.

### Methods

We included 9 FHM patients with known mutations in the CACNA1A and ATP1A2 genes and 10 healthy controls. All subjects received intravenous infusion of CGRP (1.5 µg/min).

### We recorded

Headache intensity on a verbal rating scale; mean flow velocity in the middle cerebral artery (V<sub>meanMCA</sub>) by transcranial Doppler; diameter of the superficial temporal artery (STA) by Dermascan.

### Results

CGRP-infusion did not induce an aura in any of the participants. The incidence of reported migraine and migraine-like headache was not different in the two groups, with 22% (2 out of 9) reporting migraine in the patient group, and 10% (1 out of 10) reporting migraine-like headache in the control group (-0.31 to 0.55, 95% CI) ( $P = 0.58$ ). The headache severity and intensity was not different between the groups, and we found no arterial hypersensitivity in FHM patients compared to controls.

## **Conclusion**

FHM patients do not show hypersensitivity of the CGRP-cAMP pathway, as characteristically seen in migraine patients without aura. This indicates that the pathophysiological pathways underlying migraine headache in FHM may be different from the common types of migraine and questions whether CGRP-antagonists would be effective in the management of FHM patients.

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- 1) Danish Headache Center and Department of Neurology, Glostrup Hospital, Faculty of Health Sciences, University of Copenhagen, DK-2600 Glostrup, Copenhagen, Denmark.
  - 2) Department of Pediatrics, Glostrup Hospital, Faculty of Health Sciences, University of Copenhagen, DK-2600 Glostrup, Copenhagen, Denmark.

## Body mass index positively correlated with frontal 5-HT<sub>2A</sub> receptor binding in humans

*Erritzoe D.<sup>1</sup>, Frokjaer V.G.<sup>1</sup>, Marner L.<sup>1</sup>, Svarer C.<sup>1</sup>, Madsen J.<sup>2</sup>, Baare W.<sup>3</sup>, Knudsen G.M.<sup>1</sup>*

### Introduction

Disturbances in the distribution and/or gene regulation of the postsynaptic 5-HT<sub>2A</sub> receptor are suspected to be implicated in the pathophysiology of conditions such as obesity, anorexia nervosa and bulimia nervosa.

The purpose of this Positron Emission Tomography (PET) study was to test whether body mass index (BMI) of healthy human subjects is associated with changes in the frontal cortical 5-HT<sub>2A</sub> receptor binding.

### Materials and methods

56 healthy volunteers (age: 34.0±15.8, 18 females) were investigated with [<sup>18</sup>F]-altanserin PET and 3T MRI. Subjects were either normal weighted (BMI:18.5-24.9, n=36) or overweight (BMI: 25-29.9). The steady-state binding potential, BP<sub>p</sub>, was determined using cerebellum as a reference region and metabolite corrected plasma concentration.

BMI was correlated to the 5-HT<sub>2A</sub> receptor binding with adjustment for age and neuroticism score using a multiple linear regression analysis with the regional 5-HT<sub>2A</sub> binding as the dependent variable.

### Results

BMI was positively correlated with 5-HT<sub>2A</sub> binding in frontal cortex ( $r=0.27$ ,  $p=0.048$ ).

### Conclusion

In this study, BMI was found to be positively related to 5-HT<sub>2A</sub> binding in frontal regions. Whether this change is a primary pathophysiological factor in obesity or is secondary to altered central levels of serotonin needs to be examined in future studies.

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- 1) Neurobiology Research Unit and Center for Integrated Molecular Brain Imaging, University Hospital Rigshospitalet, Copenhagen, Denmark
  - 2) PET and Cyclotron Unit, University Hospital Rigshospitalet, Copenhagen, Denmark
  - 3) Danish Center for Magnetic Resonance Imaging and Center for Integrated Molecular Brain Imaging, Hvidovre University Hospital, Denmark

## Binge Drinking during Pregnancy and Risk of Seizures in Childhood

Yuelian Sun, MD<sup>1</sup>, Katrine Strandberg-Larsen, MSc<sup>2</sup>, Mogens Vestergaard, PhD<sup>1,3</sup>, Jakob Christesen, PhD<sup>4</sup>, Anne-Marie Nybo Andersen, PhD<sup>5</sup>, Morten Grønbaek, PhD<sup>2</sup>, Jørn Olsen, PhD<sup>6</sup>

### Context

Animal studies indicate that high prenatal exposure to alcohol increase the susceptibility to seizures, but human studies are few and conflicting.

### Objective

To examine whether binge drinking during specific gestational time windows increases the risk of neonatal seizures, epilepsy, and febrile seizures.

### Design, Setting, and Participants

We conducted a population-based cohort study of 80,526 singletons from the Danish National Birth Cohort (DNBC, 1996-2002). We obtained information on binge drinking (intake of five or more drinks on a single occasion) by computer assisted telephone interviews. Children diagnosed with neonatal seizures, epilepsy, or febrile seizures as inpatients or outpatients were retrieved from the Danish National Hospital Register. Children were followed for up to eight years.

### Main Outcome Measure

Incidence rate ratio (IRR) of neonatal seizures, epilepsy, and febrile seizures in childhood.

### Results

All binge drinking episodes combined during pregnancy were not associated with an increased risk of seizure disorders, but children exposed to binge episodes between 11 and 16 gestational weeks had an increased risk of neonatal seizures (IRR, 3.15; 95% CI, 1.37-7.25) and epilepsy (1.81, 1.13-2.90).

### Conclusion

Our finding suggests that a high alcohol intake during pregnancy may have a time specific effect on the risk of some seizure disorders in the offspring.

- 1) Department of Epidemiology, Institute of Public Health, University of Aarhus, Aarhus, Denmark
- 2) Center for Alcohol Research, National Institute of Public Health, Copenhagen, Denmark
- 3) Department of General Practice, Institute of Public Health, University of Aarhus, Aarhus, Denmark
- 4) Department of Neurology and Department of Clinical Pharmacology, Aarhus University Hospital, Aarhus, Denmark
- 5) Epidemiology, Department of Public Health, University of Southern Denmark, Odense, Denmark
- 6) School of Public Health, Department of Epidemiology, University of California at Los Angeles, Los Angeles, CA, USA

## Abnormal Hemodynamic Response to Tilt Table Test in Patients With Complex Regional Pain Syndrome

Astrid J. Terkelsen<sup>1</sup>, Henning Mølgaard<sup>2</sup>, John Hansen<sup>3</sup>, Nanna B. Finnerup<sup>1</sup>, Troels S. Jensen<sup>1</sup>

### Aim

Complex Regional Pain Syndrome (CRPS) is a chronic pain condition with autonomic abnormalities in the affected limb. Our aim was to determine by tilt test whether systemic hemodynamic measures are affected in CRPS.

### Material

Twenty CRPS patients (12 F, 8 M, mean age 43.1 years) and 20 healthy age-, gender-, and BMI-matched controls were included.

Methods: Hemodynamic parameters: Mean RR, systolic and diastolic blood pressure, stroke volume, cardiac output, total peripheral resistance, heart rate variability, respiration, and baroreceptor sensitivity were continuously measured during tilt testing: 10 min in supine position, 20 min in upright position (60 degrees), and 10 min supine recovery. Moreover, heart rate variability was measured during 5 min of rest and during 5 min of arithmetic stress.

### Preliminary results

In CRPS patients as compared to controls, heart rate was significantly higher and heart rate variability tended to be reduced without affecting baroreceptor sensitivity and blood pressure. Tilt testing reduced stroke volume significantly more in patients than in controls leading to an abnormal fall in cardiac output during tilt test in patients.

### Conclusion

CRPS patients have an abnormal hemodynamic response to tilt test. We therefore conclude that CRPS affecting one extremity induces global systemic hemodynamic dysfunction.

### Acknowledgements

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1) Dept. of Neurology and Danish Pain Research Center, Aarhus University Hospital, Denmark

2) Dept. of Cardiology, Aarhus University Hospital, Skejby, Denmark

3) Center for Sensory-Motor Interaction, Aalborg University, Denmark

## **Poster session 2008**

- 1. Idiopathic intracranial hypertension and venous thrombophilia  
– a Case-control Study of Risk Factors**
- 2. Long term risk of epilepsy after thrumatic brain injury in children and young adults  
– a Population-based cohort study**
- 3. Central pain after experimental spinal cord injury (sci): histological characterisation**
- 4. Neck artery dissection and symptomatic headache mimicking primary headache types**
- 5. Separation of pain and reflex responses in an animal model of spinal cord injury**
- 6. LRRK2 G2019S point mutation screening of Danish subjects with Parkinson's Disease and Atypical Parkinsonian Syndromes**
- 7. A postal survey on post-stroke pain**

## **Idiopathic Intracranial Hypertension and Venous Thrombophilia – a Case-control Study of Risk Factors**

### **Objectives**

Idiopathic intracranial hypertension (IIH) is a condition of increased intracranial pressure of unknown pathology predominantly seen in obese young women. A more frequent predisposition to venous thrombosis in IIH has recently been reported. Coagulation abnormalities linked to the obese phenotype itself was not considered. Existing but inconsistent imaging methods may also have failed to demonstrate underlying venous pathology and it is unclear whether subjects with intracranial hypertension secondary to venous thrombosis have been excluded in previous studies.

Our aim was to examine thrombophilic parameters in a well-defined IIH population and a control population of identical demography.

### **Methods**

Prothrombotic abnormalities among 19 IIH patients with normal MRV and MRI were compared with 15 healthy sex-, age- and BMI-matched controls.

Biochemical markers tested were: homocysteine, protein C activity, total protein S antigen, antithrombin III activity, coagulation factor VIII activity, activated partial thromboplastin time, lupus anticoagulant (DRV), anticardiolipin antibodies, G1691A Leiden genotype, antinuclear antibody screening and androgen hormones.

### **Results**

Median BMI was 29.8 kg/m<sup>2</sup> (range 20.4 - 48.8 kg/m<sup>2</sup>) in cases and 26.4 kg/m<sup>2</sup> (range 20.2 - 42.6 kg/m<sup>2</sup>) in controls,  $p > 0.2$ . No single parameter differed significantly between cases and controls (Fisher's exact test, Mann-Whitney test). 10 of 19 cases (53%) and 8 of 15 controls (53%) had one or more abnormal test result.

### **Conclusion**

The present controlled study does not support hypercoagulability in IIH. Although based on a small population a significant difference between cases and controls should be expected if coagulation abnormalities were of importance in IIH. Other neurobiological mechanisms should be identified.

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## **Long Term Risk of Epilepsy after Traumatic Brain Injury in Children and Young Adults – a Population-based Cohort Study**

*Jakob Christensen, Marianne G. Pedersen, Carsten B. Pedersen, Per Sidenius, Jørn Olsen and Mogens Vestergaard,*

### **Purpose**

To estimate the long term risk of epilepsy following traumatic brain injury in Denmark.

### **Methods**

We used the Danish Civil Registration System to identify all persons born in Denmark between 1977 and 2002 (N = 1,605,216 persons) and the Danish National Hospital

Register to identify all persons treated for traumatic brain injury and epilepsy. We categorised traumatic brain injury into 1) mild brain injury (concussion), 2) severe brain injury (structural brain injury), and 3) skull fractures.

### Results

We identified 73,326 persons with mild brain injury, 3,850 persons with severe brain injury and 5,099 persons with skull fracture during 19,527,337 person-years of follow-up. There was an increased relative risk (RR) of epilepsy following mild brain injury (RR = 2.22, 95% Confidence Interval (95% CI): 2.07 – 2.38); severe brain injury (RR = 7.40, 95% CI: 6.16 – 8.89), and skull fractures (RR = 2.17, 95% CI: 1.73 – 2.71).

### Conclusion

This study shows that traumatic brain injury is a significant risk factor for development of epilepsy even following mild brain injury, many years after the injury.

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## Central Pain After Experimental Spinal Cord Injury: Histological Characterisation

*Camilla Mærsk-Møller, Danish Pain Research Center, Aarhus Univ Hospital, Aarhus Denmark, camilla.marsk-moller@studmed.au.dk; Cathrine Baastrup, Danish Pain Research Center, Aarhus Univ Hospital, Aarhus, Denmark, cathrine.baastrup@ki.au.dk; Jens Randel Nyengaard, Stereology and EM Research Laboratory and MIND Center, Aarhus University, Aarhus, Denmark, nyengaard@ki.au.dk; Nanna B. Finnerup, Danish Pain Research Center, Aarhus Univ Hospital, Aarhus, Denmark, finnerup@ki.au.dk; Troels S. Jensen, Danish Pain Research Center, Aarhus Univ Hospital, Aarhus, Denmark, tsjensen@ki.au.dk. Sponsor: Troels S. Jensen.*

### Aim

*50% of the traumatic Spinal Cord Injury (SCI) patients develop chronic neuropathic pain, which is difficult to treat. Little is known about the mechanisms underlying the development of neuropathic pain. The aims are (a) to characterize the lesion histologically and (b) to investigate predictors of chronic neuropathic pain by looking at the at- and below-level pain behavior compared to the lesion volume and the involvement of grey matter.*

### Methods

Twelve weeks following a spinal cord contusion with the MASCIS (Multi Animal Spinal Cord Injury Study) Impactor and weekly motor- and behavioral tests, the rats are euthanized. The spinal cord and brain are fixated by transcardial perfusion. The tissue is then further fixated and processed and a histological and stereological characterization of the spinal cord lesion by systematic uniform randomized sampling of the frozen tissue sections is made. Cavalier's principle and a 2D nucleator are used for estimating the volume of the lesion and the lesion of dorsal grey matter. Specific colored neurons and glial cells are counted with the optical fractionator in varying sample fractions. The individual volume of a sample of cells is found by using vertical and isotropic sections and a 3D rotator.

### Results

Will be presented.

### Acknowledgments

The Danish Agency for Science, Technology and Innovation.

## Neck artery dissection and symptomatic headache mimicking primary headache types

*Magyari M, Andree Vibeke, Ashina M, Iversen HK.*

Dissection of the carotid and vertebral arteries are now recognized as relatively common causes of strokes, particularly among young patients. We surprisingly observed patients with dissections presenting with first attack of headaches fulfilling the International Headache Society Criteria for the different primary headaches, - migraine with and without aura, cluster headache and tension-type headache.

The aim of the present study was to describe the headache types before, at onset and after neck artery dissection.

Twenty cases of dissection in the internal carotid (17) and vertebral (3) arteries were evaluated in a retrospective study of 8 women and 12 men, mean age 47.5 years (range 34-63 years).

Clinical manifestations, headache location, intensity and characteristics were registered. After at least 6 month after onset, a structured telephone interview was performed to register the present headache pattern.

The data have been collected and will be presented and discussed.

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## Separation of Pain and Reflex Responses in an Animal Model of Spinal Cord Injury

*Cathrine S. Baastrup, Danish Pain Research Center, Aarhus University, Aarhus, Denmark, cathrine.baastrup@ki.au.dk; Camilla Maersk-Moeller, Danish Pain Research Center, Aarhus University, Aarhus, Denmark, camilla.maersk-moeller@studmed.au.dk; Nanna B. Finnerup, Danish Pain Research Center, Aarhus University Hospital, Aarhus, Denmark, Finnerup@ki.au.dk; Troels S. Jensen, Danish Pain Research Center, Aarhus University Hospital, Aarhus, Denmark, tsjensen@ki.au.dk. Sponsor: Cathrine S. Baastrup*

### **Aim of investigation**

To separate the spinal reflex behaviour from supraspinal responses following stimulation with von Frey filaments in the spinal cord contusion animal model.

- The spinal cord contusion (SCC) model is an experimental animal model of spinal cord injury with good mechanistic congruence to the clinical picture of a traumatic spinal cord injury. The model has a high morphological and injury-related reproducibility and has produced evoked below-level neuropathic pain in previous pain studies, though with variable incidence and severity.
- A standard evaluation paradigm for evoked below-level pain in animals is the paw withdrawal (PW) of the hind limb in response to mechanical stimulation with von Frey filaments. Therefore, a description of the nature of the PW is important.
- The SCC animals develop spontaneous and evoked spasms of the hind limbs, e.g. in response to light stimulation of the skin, equivalent to spinal cord injured patients. The stimulation and the spasm are not necessarily felt as painful or even felt at all, but would be scored as pain using the PW criteria, at the risk of bias.

A cerebrally evoked pain response may also be modulated differently from the spinal reflex. It is therefore important to separate a cerebrally mediated pain response from a spinal or brainstem reflex behaviour.

### Methods

The study is randomized and blinded. SCC is performed on 200 g male Sprague-Dawley rats at T9-10 using a 25 mm drop of a 10 g rod unto the exposed medulla. Mechanical stimulation intended to evoke pain by von Frey filaments in an up-down paradigm

1. Comparison of the development and duration of responses evaluated by simple PW or supraspinal response criteria (orientation, vocalization, or escape)(N=22)
2. Comparison of responses after treatment (0-180 min.) with a. Baclofen 0.5 mg/kg (spasmolytic), b. Pregabalin 50 mg/kg (analgesic), and c. Saline 0.9% (N=8)

### Results

No below-level pain was detected in the SCC animals evaluated by the supraspinal response criteria during 8 weeks of measurement of the von Frey threshold.

The sham-animals (N=7) have significantly lower threshold the SCC animals (N=15)( $p=0.0113$ ), suggesting hypo-sensibility or decreased motor coordination and function.

### Conclusion

The study is on going and results will be presented during poster session on site.

### Acknowledgements

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## LRRK2 G2019S point mutation screening of Danish subjects with Parkinson's Disease and Atypical Parkinsonian Syndromes

*Sara Bech, MD, Anne Nørremølle, PhD, Kristian Winge, MD, PhD,*

*Lena Hjermind, MD, PhD*

Mutations in the leucine-rich repeat kinase 2 gene (LRRK2) are the most common cause of autosomal dominantly inherited Parkinson's disease (PD). LRRK2 spans 51 exons and encodes a 2527 amino acid protein, the precise function of which is undetermined. Numerous point mutations have been identified across the gene, the frequencies of which vary among different ethnic groupings. The Gly2019Ser point mutation on exon 41 is the most prevalent identified to date among Caucasians, however, the frequency in the Danish PD population is unknown. The phenotype in the LRRK2 PD is most often indistinguishable from the sporadic form with late onset and good levodopa response. Studies of LRRK2 mutations in Atypical Parkinsonian Syndromes (APS) are lacking.

### Patients and Methods

250 PD (with and without family history) and 50 APS patients were screened for the G2019S mutation, assayed by SfiI digestion of the PCR product. Bi-directional DNA sequencing using standard methods confirmed mutations.

### Results

Few mutations were found.

### Discussion

The identification of so few G2019S mutations may be due to either other LRRK2 mutations being predominant, or LRRK2 PD being rare in Denmark. Consequently we cannot extrapolate epidemiological genetic results from otherwise comparable populations.

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## A Postal Survey on Post-Stroke Pain

*H. Klit<sup>1</sup>, N.B. Finnerup<sup>1</sup>, K. Overvad<sup>2</sup>, G. Andersen<sup>3</sup>, T.S. Jensen<sup>1,3</sup>*

### Background

Chronic pain after stroke, such as hemiplegic shoulder pain and central post-stroke pain, is common. The objective of the study is to assess pain prevalence in post-stroke patients and in a reference group.

### Method

All surviving stroke patients (N=964, F=457, M=507), registered in the National Indicator Project (NIP) stroke database in Aarhus County, Denmark, between March 2004 and February 2005, were mailed a questionnaire about the development of chronic pain after stroke onset. A sex- and age-matched reference group (N=957, F=456, M=501) served as control.

### Results

Mean age of stroke subjects and controls was 70.9 and 69.6 years ( $p=0.89$ ) and male ratio was 55.3% and 58.3% ( $p=0.3$ ), respectively. Response rates were 66.5% (643) and 59.5% (570) ( $p<0.05$ ), respectively.

Development of chronic pain (38.7% vs 28.9%), chronic headache (10.9% vs 2.3%), shoulder pain (15.2% vs 9.8%), pain from spasticity (17.2% vs 5.3%), other pain (20.4% vs 12.9%) and high LANSS score, suggesting neuropathic pain (10.1% vs 3.9%), were significantly more common in the stroke group.

### Conclusion

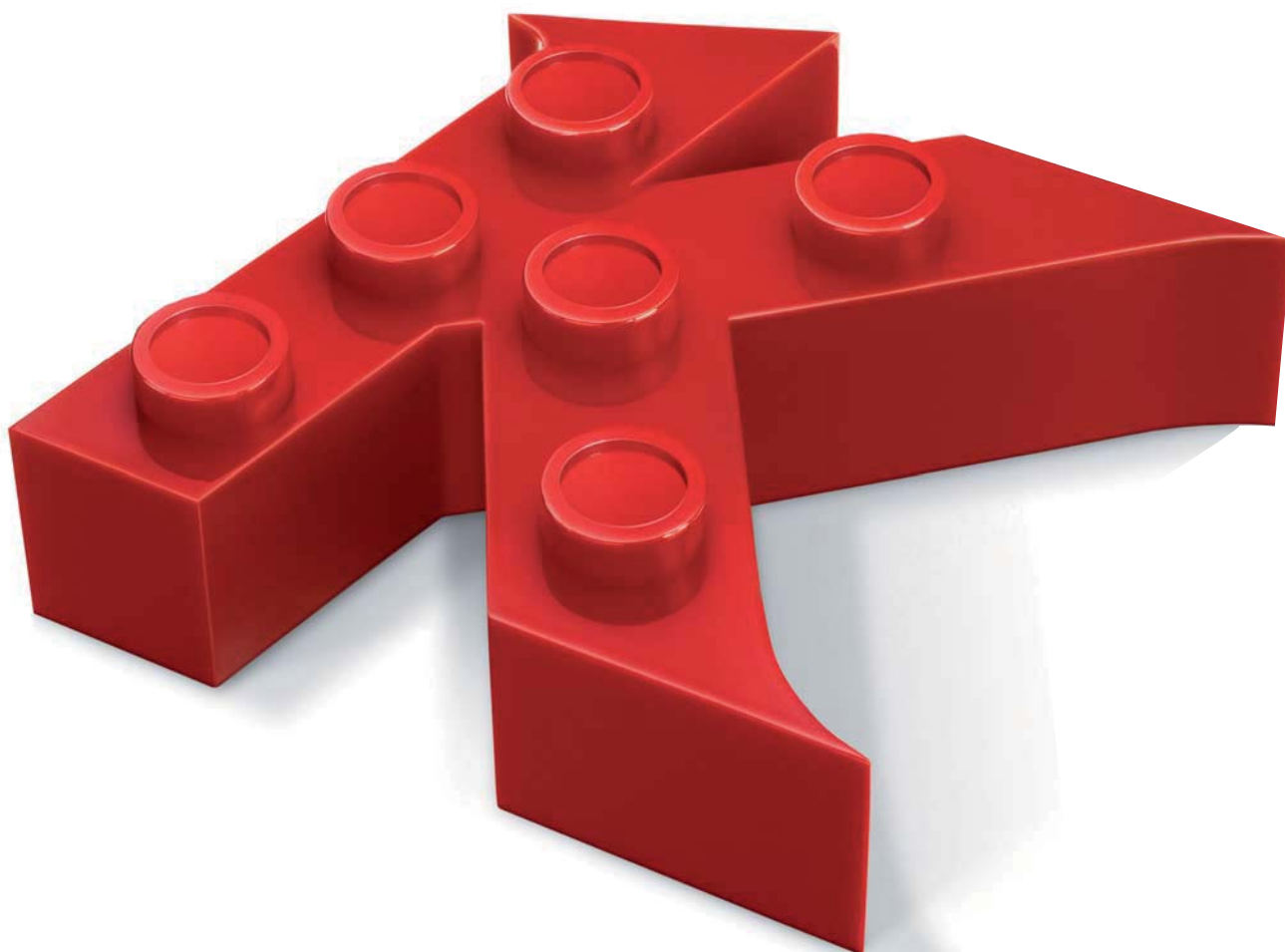
Chronic headache, shoulder pain, neuropathic pain, and pain from spasticity is more common in stroke patients than in an age- and sex-matched control group.

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1) Danish Pain Research Center

2) Department of Clinical Epidemiology, Aarhus University Hospital, Aalborg

3) Department of Neurology, Aarhus University Hospital, Aarhus



## Keppra, levetiracetam

**Indikationer:** Monoterapi behandling af nydiagnosticerede patienter over 16 år med partiel epilepsi med eller uden sekundær generalisering. Tillægsbehandling af voksne og børn over 4 år med partiel epilepsi med eller uden sekundær generalisering. Tillægsbehandling af voksne og unge over 12 år med juvenil myoklon epilepsi med myoklone anfald. Tillægsbehandling af voksne og unge over 12 år med Idiopatisk Generaliseret Epilepsi med primære generaliserede toniske-kloniske anfald. **Dispenseringsformer:** Tabletter à 250 mg, 500 mg, 750 mg eller 1000 mg levetiracetam. Oral opløsning. 1 ml indeholder 100 mg levetiracetam. Levetiracetam koncentrat til infusionsvæske, 100 mg/ml opløsning i 5 ml hætteglas. **Dosering og indgivelsesmåde:** De filmovertrukne tabletter indtages peroralt, synkes med en tilstrækkelig mængde væske, og kan indtages med eller uden føde. Den orale opløsning skal opløses i et glas vand, og kan indtages med eller uden føde. Keppra koncentrat til intravenøs anvendelse skal fortyndes i mindst 100 ml af en kompatibel fortynder. Infusionen skal indgives over 15 min. Den daglige dosis bør indtages i to ligeligt fordelte doser. **Monoterapi: Voksne og unge over 16 år:** Den anbefalede begyndelsesdosis er 250 mg to gange daglig som efter 2 uger øges til en initial terapeutisk dosis på 500 mg to gange daglig. Dosis kan øges med yderligere 250 mg to gange daglig hver anden uge afhængig af den kliniske effekt. Den maksimale dosis er 1500 mg to gange daglig. **Tillægsbehandling: Voksne (≥ 18 år) og unge (12 til 17 år) som vejer 50 kg eller mere:** Den initiale, terapeutiske dosis er 500 mg to gange daglig. Man kan starte med denne dosering fra den første behandlingsdag. Afhængig af klinisk effekt og tolerabilitet kan den daglige dosis øges til 1500 mg to gange daglig. Ændring af dosis kan gennemføres med forøgelse eller reduktioner på 500 mg to gange daglig hver anden til fjerde uge. Ældre (65 år og ældre). Justering af dosis anbefales hos ældre patienter med nedsat nyrefunktion (se "Patienter med nedsat nyrefunktion" nedenfor). **Børn fra 4 til 11 år og unge (12 til 17 år) som vejer mindre end 50 kg:** Den initiale, terapeutiske dosis er 10 mg/kg to gange daglig. Afhængig af klinisk effekt og tolerabilitet kan den daglige dosis øges op til 30 mg/kg to gange daglig. Ændring af dosis kan gennemføres med forøgelse eller reduktioner på højst 10 mg/kg 2 gange daglig hver anden uge. Den laveste, effektive dosis bør anvendes. Dosis til børn, der vejer 50 kg eller mere, er den samme som hos voksne. Lægen bør ordinere den mest anvendelige lægemiddelform og styrke afhængig af vægt og dosis. **Spædbørn og børn under 4 år:** Keppra er ikke anbefalet til brug hos børn under 4 år p.g.a. utilstrækkelige data vedrørende effekt og sikkerhed. **Patienter med nedsat nyrefunktion:** Se fuldstændigt produktresumé (rekvirering se nedenfor). **Patienter med nedsat leverfunktion:** Se fuldstændigt produktresumé (rekvirering se nedenfor). **Kontraindikationer:** Overfølsomhed over for levetiracetam eller andre pyrrolidon derivater et eller flere af hjælpestofferne. **Særlige advarsler og forsigtighedsregler vedrørende brugen:** I overensstemmelse med nuværende klinisk praksis anbefales det, at Keppra, hvis behandlingen skal afbrydes, seponeres gradvist (f.eks. for voksne: reduktion med 500 mg to gange daglig hver anden til fjerde uge; for børn: dosis bør ikke reduceres med mere end 10 mg/kg to gange daglig hver anden uge). Tilgængelige data for børn tyder ikke på indflydelse på vækst og pubertet. Men langvarig indvirken på indlæring, intelligens, vækst, endokrin funktion, pubertet, og indvirken på evnen til at få børn er ukendt. En forøgelse af anfaldsfrekvensen på mere end 25 % blev rapporteret hos 14% af levetiracetam-behandlede voksne og pædiatriske patienter med anfald af partiel type, hvorimod det blev rapporteret hos henholdsvis 26% og 21% af placebo-behandlede voksne og pædiatriske patienter. Anvendelse af Keppra til patienter med nedsat nyrefunktion kan kræve dosisjustering. Hos patienter med svært nedsat leverfunktion anbefales bestemmelse af nyrefunktion for valg af dosis. Keppra 750 mg filmovertrukne tabletter indeholder farvestoffet E110 som kan give allergiske reaktioner. Keppra 100 mg/ml oral opløsning indeholder metylparahydroxybenzoat (E218) og propylparahydroxybenzoat (E216) som kan medføre allergiske reaktioner (muligvis forsinket). Opløsningen indeholder også maltitol; patienter med fructosintolerans som er et sjældent arveligt problem bør ikke tage dette lægemiddel. **Interaktion med andre lægemidler og andre former for interaktion:** Præ-marketing data fra kliniske undersøgelser med voksne tyder på, at Keppra ikke påvirker serumkoncentrationerne af eksisterende anti-epileptika (fenytoin, karbamazepin, valproat, phenobarbital, lamotrigin, gabapentin og primidon), og at disse anti-epileptika ikke påvirker Keppra's farmakokinetik. Absorptionen af levetiracetam blev ikke ændret ved fødeindtagelse, men absorptionshastigheden blev lettere reduceret. Der foreligger ikke data over interaktion af levetiracetam og alkohol. **Graviditet og amning:** Der foreligger ikke tilstrækkelige data ved brug af Keppra hos gravide kvinder. Undersøgelser på dyr har vist reproduktiv toksicitet (se afsnit 5.3). Den potentielle risiko for mennesker kendes ikke. Keppra bør ikke anvendes under graviditet, medmindre det er absolut nødvendigt. Afbrydelse af behandling med anti-epileptika kan medføre forværring af sygdommen, der kan være skadelig for moderen og fosteret. Levetiracetam udskilles i human modermælk. Derfor anbefales amning ikke. **Virknin-ger på evnen til at føre motorkøretøj eller betjene maskiner:** Da der er risiko for bl.a. somnolens og svimmelhed, tilrådes forsigtighed ved bilkørsel og maskinbetjening. Patienter rådes til ikke at føre motorkøretøj eller betjene maskiner, før det er bevist, at deres evne til at udføre sådanne aktiviteter ikke er påvirket. **Bivirkninger:** Rapporteret i kliniske afprøvninger (børn og voksne) samt erfaring efter markedsføring er: Meget hyppige bivirkninger (>1/10): asteni, træthed, somnolens. Hyppige bivirkninger (>1/100, <1/10): amnesi, ataksi, krampe, svimmelhed, hovedpine, hyperkines, tremor, balanceforstyrrelse, koncentrationssvækkelse, hukommelsessvækkelse, agitation, depression, emotionel labilitet, humørsvingninger, fjendtlighed, aggression, søvnløshed, nervøsitet, irritabilitet, personlighedsforstyrrelse, abnorm tænkning, mavesmerter, diarré, dyspepsi, kvalme, opkastning, anoreksi (risikoen for anoreksi er større, når topiramet gives samtidig med levetiracetam), vægtøgning, vertigo, diplopi, sløret syn, myalgi, skader ved uheld, infektion, nasopharyngitis, forværret hoste, hud-udslæt, eksem, pruritus, trombocytopeni, **Erfaring efter markedsføring:** Paræstesi, unormal adfærd, vrede, angst, forvirring, hallucinationer, irritabilitet, psykotisk lidelse, selvmord, selvmordsforsøg og selvmordstanker, alopeci (i flere tilfælde blev der set bedring af tilstanden, når Keppra blev seponeret), leukopeni, neutropeni, pancytopeni. **Overdosering: Symptomer:** Somnolens, agitation aggression, nedsat bevidsthed, respirationshæmning og koma blev set ved overdosering med Keppra. **Behandling af overdosering:** Efter en akut overdosis bør maven tømmes med hjælp af maveskyllning og induktion af opkastning. Der kendes ingen specifik antidot for levetiracetam. Behandling af overdosering er symptomatisk og kan omfatte hæmodialyse. Effektiviteten ved dialyse-ekstraktion er 60 % for levetiracetam og 74% for den primære metabolit. **INDEHAVER AF MARKEDSFØRINGSTILLADELSEN:** UCB S.A., Allée de la Recherche 60, B-1070 Bruxelles, Belgien. **Udlevering, pakninger, priser og tilskud (AUP marts 2007):** Filmovertrukne tabletter: 250 mg, 50 stk. kr. 384,40, 100 stk. kr. 747,35; 500 mg, 100 stk. kr. 1322,60, 200 stk. kr. 2599,45; 750 mg, 100 stk. kr. 2088,70; 1000 mg, 100 stk. kr. 2501,10, 200 stk. kr. 5096,15; oral opløsning 100 mg/ml kr. 1597,15; koncentrat til infusionsvæske 100mg/ml 10 x 5 ml. kr. 2072,50. **Forkortet i forhold til det godkendte produktresumé, der kan rekvireres fra: UCB Nordic A/S, Arne Jacobsens Allé 15, 2300 København S.**

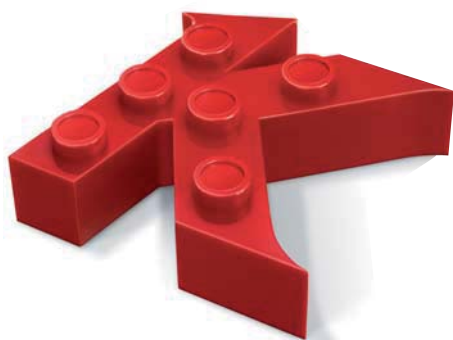


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