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VNS Therapy

Facing the Real Challenges of Difficult-to-treat Epilepsy

VNS Therapy

Facing the Real Challenges of Difficult-to-treat Epilepsy

1. Facing Difficult-to-treat Epilepsy

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2. Living with VNS Therapy

Mrs. Cathy Queally; King's College Hospital – United Kingdom

3. Questions and Answers

VNS Therapy

Facing the Real Challenges of Difficult-to-treat Epilepsy

Facing Difficult-to-treat Epilepsy

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Reference Center for Refractory Epilepsy



Laboratory for Clinical and Experimental Neurophysiology





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Facing Difficult-to-treat Epilepsy

Definition and Prevalence

Difficult-to-treat Epilepsy

Definition and Prevalence

- **Definition**

- There is no single definition
- Failure of two appropriate anti-epileptic drugs
- High seizure frequency
- No long seizure-free periods

- **Prevalence**

- Epilepsy: 0,5 – 1% of the population
- 2/3 of the epilepsy patients become seizure-free with one or two anti-epileptic drugs
- Difficult-to-treat epilepsy: 1/3 of the epilepsy patients

Difficult-to-treat Epilepsy

Definition

- **No or little response to anti-epileptic drugs**
→ obtaining seizure freedom becomes difficult
 - **Increased health risk**
 - **Impact on social functioning and professional life**
 - **Mood disorders**
 - **Side effects of multiple drug treatment**
(concentration, tiredness,...)
- **Quality of life is affected!**



Facing Difficult-to-treat Epilepsy

Treatment Options

Difficult-to-treat Epilepsy

Treatment Options

- **New anti-epileptic drugs, clinical trials**
 - 4% seizure freedom¹
 - Side-effects
- **Epilepsy surgery**
 - 60-70% seizure freedom
 - Risk of surgery
 - Minority of patients are good candidates (<10%)
- **Ketogenic diet**
 - Side-effects
 - Difficult to maintain
- **VNS Therapy**

1. Kwan and Brodie, NEJM 2002



Facing Difficult-to-treat Epilepsy

VNS Therapy

VNS Therapy

Indication for use

- A treatment option for surgically and/or medically refractory epilepsy
- Indication for use in Europe and Canada
 - VNS Therapy is indicated as an **adjunctive therapy** for epilepsy patients with **partial seizures** (with or without secondary generalisation) or **generalised seizures**, which are **refractory to anti-epileptic medications**
 - Both for adults and children

VNS Therapy

How does it work?

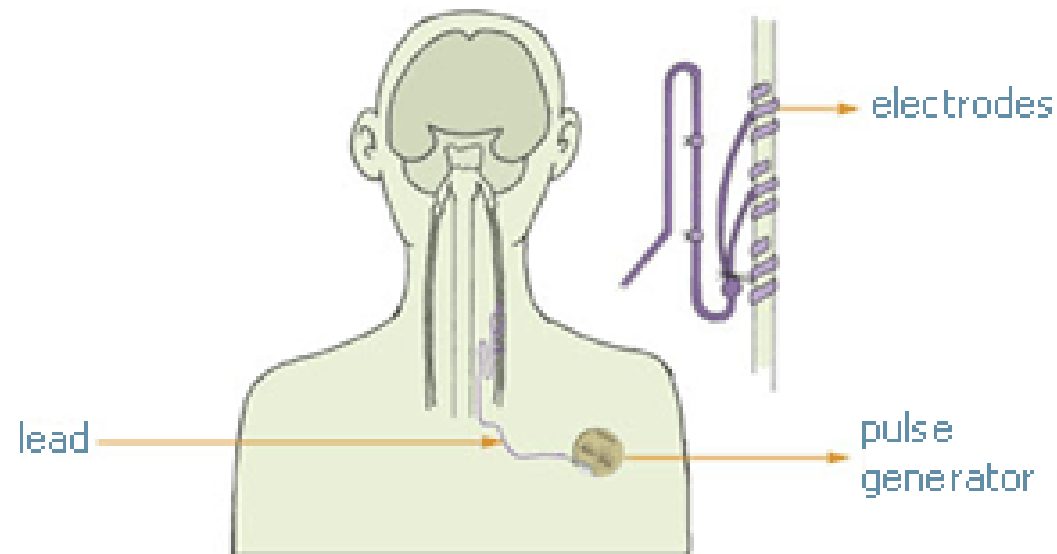
- VNS Therapy uses a small medical device (the pulse generator) that sends small electrical pulses to the left vagus nerve in the neck
- The vagus nerve is a major communication link between the body and the brain
- The vagus nerve delivers these electrical pulses to the brain
- VNS Therapy helps to prevent the electrical irregularities that cause seizures



VNS Therapy

How does it work?

- ⇒ **Continuous (24h/d), intermittent (on/off) electrical stimulation** of the left **vagus** nerve by means of
1. A helical **electrode** wound around the left vagus nerve and
 2. An implantable, programmable pulse **generator** located subclavicularly



VNS Therapy

How does it work?

- **Stimulation parameters:**
 - On / Off cycle (sec/min)
 - Pulse width (micro-sec)
 - Frequency (Hz)
 - Stimulation output (mA)
- **Gradually increase in output, start 2-4 weeks after implantation**



VNS Therapy

Side-effects

- **Implantation related side-effects**
 - Infection (3-6%)
 - Vocal cord paresis (rare)
- **Stimulation related side-effects (15-20%)**
 - Coughing, hoarseness or other voice alteration, painful sensation in the throat, shortness of breath
 - Mild
 - Respond to changes of the stimulation settings
 - Tend to decrease over time

VNS Therapy

Seizure Reduction in Adults

- **Seizure reduction in adults**
 - **Two randomized, controlled, double-blind, multicenter studies (E03 and E05)**
 - **Long-term follow-up study in 440 patients:**
After one year of VNS Therapy : 37% of the patients had 50% or more reduction in the frequency of their seizures¹.
This percentage increased to 43% after 2 years of stimulation¹

VNS Therapy

Seizure Reduction in Children

- **Seizure reduction in children**
 - **Prospective open safety study¹**
 - 60 children (3 - 18 years)
 - Various epilepsy types
 - 42% seizure reduction after 18 months
 - **Retrospective multi-centre study²**
 - 95 children
 - 44,7% seizure reduction after 6 months

1. E04 Study – 2. Helmers 2001

VNS Therapy

Seizure Types and Syndromes

- **Seizure types that benefit from VNS Therapy**
 - Simple and complex partial seizures
 - Tonic clonic seizures
- **Epilepsy syndromes that benefit from VNS Therapy**
 - Localised epilepsy¹
 - Generalised epilepsy^{2,3,4}
 - Others
 - Lennox-Gastaut^{5,6,7}
 - Tuberous sclerosis⁸
 - Progressive myoclonic epilepsy⁹

1. FDA approval 1997 - 2. EU approval - 3. Holmes 2004 - 4. Devinsky 2004 - 5. Frost 2001 - 6. Majoie 2001 - 7. Majoie 2005 –
8. Parain 2001 - 9. Smith 2000

VNS Therapy

Non-drug Therapy

- VNS Therapy has not the same side-effects as the anti-epileptic drugs
 - Tiredness
 - Dizziness
 - Concentration and memory problems
 - Drug toxicity
- Can be added to any drug
- Is indicated in any seizure type or epilepsy syndrome

VNS Therapy *Efficacy*

- **1/3 of patients have more than 50% seizure reduction**
 - E01-E05 studies, 1999, follow-up 3 years, 440 patients
 - 43% of the patients have a 50% or greater reduction in their number of seizures
- **Not only benefit in seizure frequency, but also in seizure severity and recovery**
- **Delayed but sustained efficacy**
- **Use of magnet provides additional benefits**



VNS Therapy

Quality of Life

- Overall quality of life
 - Quality of life (QoL) of 136 adults¹
 - By means of a questionnaire at baseline and after 3 months of VNS Therapy
 - Patients who experienced a 50% or greater reduction in seizures had statistically significant improvements in energy, memory, social functioning, mental health, and fear of seizures
 - Mood and overall QoL improved in patients with lesser seizure reductions

1. Cramer 2001

VNS Therapy

Quality of Life

- **Mood**
 - Mood improvement, independent of seizure reduction^{1,2}
 - Improvement of tenseness after 6 months of VNS Therapy³
- **Cognitive function**
 - Cognitive studies
 - Attention, motor functioning, short-term memory, learning, and executive functions
 - No evidence of worsened cognitive function³ was found in 36 patients before and after 6 months VNS

VNS Therapy

Quality of Life

- **Memory**
 - Significantly enhanced retention of verbal learning (word recognition)¹
- **Excessive daytime somnolence and sleep**
 - Reduction of daytime sleepiness, independent of reductions in seizure frequency²
 - Positive effect on sleep structure followed by improved quality of life³

VNS Therapy

Quality of Life

- **Developmentally disabled and mentally retarded patients**
 - Improvements in attention, clarity of speech, household tasks in patients who live in long-term care facilities⁴
 - Gain in mental age and more independent behaviour in patients with Lennox-Gastaut Syndrome⁵

4. Huf 2005 – 5. Aldenkamp 2001

VNS Therapy *Conclusions*

- **Vagus nerve stimulation is an efficacious, well-tolerated and safe therapy for patients who have difficult-to-treat epilepsy**

- **Vagus nerve stimulation has a positive impact on quality of life**

VNS Therapy

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Living with VNS Therapy

Ms. Cathy Queally

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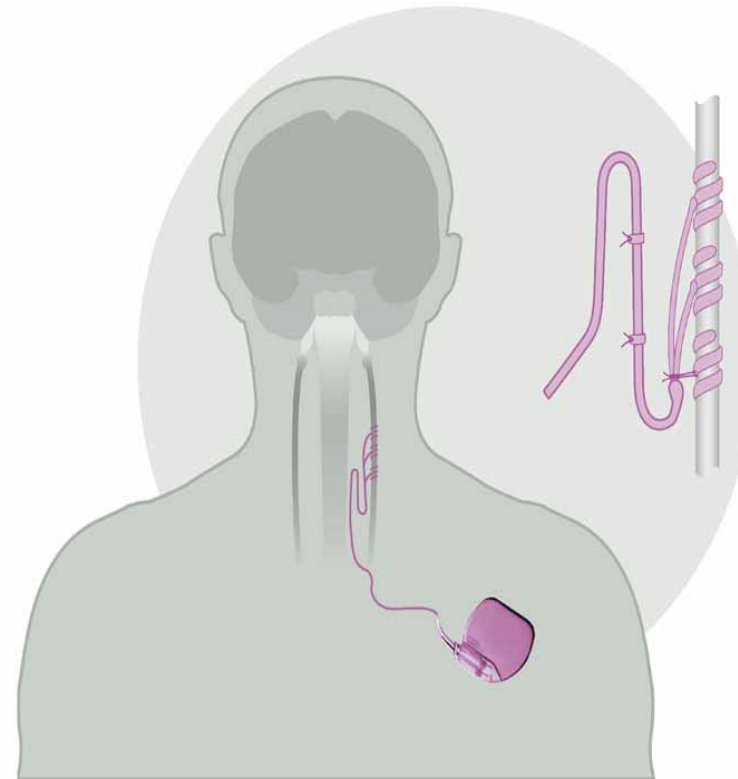
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King's College Hospital **NHS**
NHS Trust

Which Steps to Start with VNS Therapy?

VNS Therapy *Device / Implanted*



VNS Therapy *Device / Implanted*

- **Implantation of the VNS Therapy generator**
 - **Not brain surgery**
 - **Simple surgical procedure**
 - **Only a short stay in hospital**
 - **Two small incisions are made**
 - **One to place the pulse generator, under the skin **just below the left collar bone or close to the armpit****
 - **A second small incision in the **neck** to attach two tiny wires (electrodes) to the left vagus nerve.**
 - **Aside from **tiny scars**, which usually fade with time and blend in with the natural fold of the neck, and a slight bulge in the chest, the device is hardly noticeable**



VNS Therapy *Programming*



VNS Therapy *Programming*

- **Follow-up**
 - **Outpatient visits:** The doctor or nurse read and adjust the stimulation settings
 - This is **painless** and can even be done through the clothes. The device will continuously cycle as programmed by the doctor or nurse
 - A series of **follow-up visits** will be planned. Initially, they will be more frequent, to ensure the stimulation settings are optimum. Later, visits will be 1-2 per year to check the device.

Cycling Options / Magnet Use

- **Normal Cycling**

Current 0.25mA – 2.00mA
On for 30 seconds
/ Off 5 Minutes

- **Intermediate Cycling**

Current 0.25mA – 2.00mA
On for 30 Seconds
/ Off 3 Minutes

- **Rapid Cycling**

Reduce Current to a lower level
On for 7 seconds
/ Off 30 Seconds

- **Magnet use**

Swipe magnet across VNS generator to activate device to deliver an extra stimulation cycle

- Current of magnet is usually **0.25mA higher** than device current and will stimulate for **60 seconds** only

- VNS Therapy device then returns to usual settings

Living with VNS Therapy

Quality of Life Improvements

Quality of Life Improvements

Seizure Control

- Reduction in seizure number
- Reduction in seizure frequency
- Seizure occurring over a few days – clustering rather than daily
- Increase in seizure free days
- Improve a specific type of seizure only e.g. atonic

Quality of Life Improvements *Seizure Changes*

- **Length of time**
- **Intensity / Severity**
- **Recovery time**
- **Cease or dramatically reduce the activity of a specific seizure type e.g. atonic**
- **Post Seizure Behaviour**

Quality of Life Improvements

VNS Therapy Magnet

- The magnet may provide additional benefits for some people. It is not necessary to use it for regular stimulation
- By **swiping** the VNS Therapy magnet over the pulse generator the patient or caregiver **immediately activates therapy**, which can be done when the patient feels a seizure coming on or during a seizure



Quality of Life Improvements

VNS Therapy Magnet

- **Control: Build up in confidence**
- **May stop seizure activity**
- **Used in emergency seizure management: reduces need for emergency drugs/ admissions to hospital**
- **Reduces: Length of time of seizure
Seizure Intensity / Severity
Improve seizure recover time**

Quality of Life Improvements

VNS Therapy Magnet

- Can be used by family / friends / carers
- Reduces anxiety
- Patient has the ability to switch device off – Rarely needed or done

Quality of Life Improvements

Other QoL Improvements

- **Reduction in Emergency Room / A&E attendance**
- **Reduction in admission to hospital**
- **Reduction in use of emergency drugs**
- **Reduction in injuries due to seizures e.g atonic seizures - facial, chin and head injuries**

Quality of Life Improvements

Non Epilepsy QoL Improvements

- **More outgoing / interactive with people**
- **Feel more positive and happy**
- **Feel more alert and able to concentrate**
- **Easing in concerns about seizures and potential impact on life / work**

Quality of Life Improvements *Children*

- **Improved learning / concentration**
- **More interactive: Playing /class room**
- **More alert**

Quality of Life Improvements *Learning Disability Patients*

- **Behaviour can change: Good & Bad**
- **Learning / Concentration improves**
- **More alert**
- **More interactive: Asking to do things or initiating activities**

Quality of Life Improvements *Anti-Epileptic Drugs (AEDs)*

Potential to

- Reduce number of AEDs used
- Reduce dosage of AEDs
- Reduce use of emergency drugs e.g. Rectal Diazepam/
Buccal Midazolam/ Clonazepam

Living with VNS Therapy

Patients' Stories

Story of S.L.

- 27 years old woman, epilepsy since 6 years old
- Tried All AEDs – never seizure freedom
- Suitable for resective surgery but patient did not wish to proceed at this time (2002)
- VNS Therapy implanted: June 2003
- Reached maximum current 2.00mA & Tried all 3 cycling patterns over an 18 month period
- No improvement in seizure control or mood etc...
- VNS Therapy switched off in September 2005
- Device removed in March 2006

Story of H.Q.

(1)

- **HQ – aged 32 – developed Epilepsy aged 6**
- **Temporal lobe epilepsy**
 - **Seizure types: Complex-Partial Seizures & Tonic-Clonic**
 - **Seizures: 12 –14 per month**
- **Long standing personality, behavioural and personality problems requiring psychiatric care**

Story of H.Q. (2)

- **Severe Medical Intractable Epilepsy**
- **All AEDs introduced – no real improvement**
- **Epilepsy Surgery Assessment – Found not to be suitable as Bilateral temporal lobe abnormalities**
- **Nov. 1999 – VNS Therapy inserted and switched on**

Story of H.Q. (3)

- **Current from 0.25mA to 2.25mA**
- **Normal, Intermediate and Rapid cycling utilised**
- **Side effects: gastric distress, nausea & vomiting, burping and loss of appetite**

Story of H.Q. (4)

**2001 – Agreed no real improvement in seizure activity
possibly seizures less aggressive**

BUT

**Mood improvement: Considerable effect on his
demeanour and personality**

SO

**VNS Therapy switched off Jan 2002 at patient insistence
because of side effects**

Story of H.Q. (5)

SO

May 2002 – Switched back on as patient behaviour had deteriorated e.g. more irritable and argumentative

TODAY

VNS Therapy still in use – No seizure improvement but behaviour and QoL has improved

Story of G.W.

(1)

- **Epilepsy since aged 22 following Cerebral Viral Infection in 2001**
- **AEDs: All tried never full seizure control / Found not to be suitable for resective epilepsy surgery**
- **4-6 Tonic-Clonic seizures per week**
- **4-6 Complex / Simple partial seizures per day with episodes of clusters**

Story of G.W. (2)

- **Unable to complete her degree course / Unable to work**
- **Noise triggering seizures: door opening, cup lifted off table, clock ticking or voices could trigger seizures**
- **Laying in dark, quite room for days/ weeks at a time: isolated, depressed feelings of hopelessness**

Story of G.W. (3)

- **2004**
 - **5 months after VNS Therapy switched on: VNS current set at 1.25mA, On 30 seconds/ Off 5 minutes. Magnet helping**
 - **Seizures reduced to 1-2 per week : Complex partial seizures only**
 - **Noise trigger no longer a problem**
 - **Magnet helping abort complex partial seizures**
 - **No Tonic-clonic Seizures for 3 months**

Story of G.W.

(4)

2005

- **Seizure Reduction maintained: now mild partial seizures 1-2 per month**
- **No Tonic-Clonic Seizures since 2004**
- **Reduced dose of 2 AEDs: continuing on 4 AEDs**
- **Working part time also volunteer work**
- **Married - honeymoon in Australia**

2006

- **Working part time**
- **Returned to University part time to complete degree**
- **Commenced adoption process**
- **Seizure activity stable / AEDs unchanged**

Story of K.S.

(1)

- 11 years old with profound learning difficulties
- Difficult-to-treat epilepsy; multiple different seizure types
- AEDs not controlling seizures
- Unsuitable for epilepsy surgery

Story of K.S. (2)

- **VNS Therapy inserted May 2002**
- **VNS switched on 6th June 2002 on basic settings**
 - **Uncommunicative**
 - **No eye contact**
 - **Restricted mobility, wheelchair reliant**

Story of K.S. (3)

- **Parents Comments: 13th August 2002**
 - **Vast improvement in overall wellbeing**
 - **Co-ordination better**
 - **Spending less time in wheelchair**
 - **Seizure control improved, -- drop attacks not as frequent, -- going longer between major seizures, -- not having as many Jerks**
- **VNS Therapy current increased increased to next level**

Story of K.S. (4)

- **Parents Comments: 1st October 2002**
 - **Improvement in overall wellbeing maintained**
 - **Can now use a feeder cup**
 - **Hardly using wheelchair**
 - **Trying to vocalise..... Said "Hello" to headmaster at school**
 - **No fits at all for last month, (drops, jerks) no major fit since 3rd August**

Story of K.S. (5)

- **During consultation Kate was very noisy, moving unaided around the room**
- **Displaying lots of interaction, particularly with her father**
- **Engaged eye contact**
- **Responded to and played with musical toys**
- **No change was made to the stimulator**

Story of K.S. (6)

- **Review 11th February 2002**
 - **Prolonged Viral Illness in December**
 - **Marked increase in Seizure activity**
 - **Jerks and Drops only! No Tonic-Clonic seizures**
 - **Improved mobility and interaction was maintained**
 - **VNS Therapy current increased to 0.75mA**

Story of K.S.

(7)

- **May 2005**
 - Feeding tube removed
 - Intermittent bouts of increased Jerks and Drops
 - No Tonic-Clonic Seizures
 - VNS Therapy current increased to 1.0mA at parents request

- **April 2006**
 - VNS Therapy still in
 - Intermittent bouts of increased Jerks and Drops
 - No Tonic-Clonic Seizures

VNS Therapy

Conclusions

- **As a novel and unusual treatment – patients need to talk to both health care professionals and others about the device**
- **Improves communication skills, confidence and opportunity for patients to teach others about an aspect of care not experienced before**

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Questions ?