This Current Awareness Bulletin is produced by the Healthcare Library to provide Salisbury NHS Foundation Trust staff with a range of resources to support practice. It will include recently published guidelines and research articles, news and details of new library resources.

**Athens**

To access journal articles that are available in full text you will need to have a username and password for Athens. To register for an Athens account click here.

For further information or support please contact the Healthcare Library, SDH Central, Salisbury District Hospital, Salisbury, Wiltshire SP2 8BJ. 01722 429054 or 01722 336262 ext 4430, Library.office@salisbury.nhs.uk, or visit the library website at www.library.salisbury.nhs.uk

**News**

**NHS Choices**

How immunotherapy may treat multiple sclerosis
Thursday 4th September 2014

Autoimmune disorders, such as multiple sclerosis (MS), occur when the body’s immune system attacks and destroys healthy body tissue by mistake. The “holy grail” of treatment is to make the immune system tolerant to the part of the body that it is attacking, while still allowing the immune system to work effectively. A new mouse study has found that a carefully calibrated dose-escalation protocol caused changes in gene activity (gene expression). This then causes the attacking immune cells to express regulatory genes and to become suppressive. So rather than attacking healthy tissue, they are now ready to protect against further attacks against healthy tissue.

**UpToDate®**

What’s new in neurology

**Guidelines**

National Institute for Health and Care Excellence (NICE)

Dimethyl fumarate for treating relapsing-remitting multiple sclerosis

Multiple sclerosis: management of multiple sclerosis in primary and secondary care
Cochrane Systematic Reviews

New Reviews – October 2014

Antiepileptic drugs for the primary and secondary prevention of seizures in viral encephalitis

Clobazam monotherapy for partial-onset or generalized-onset seizures

New Reviews – September 2014

Comparison of antiepileptic drugs, no treatment, or placebo for children with benign epilepsy with centro temporal spikes

Desipramine for neuropathic pain in adults

Updated Reviews – September 2014

Anticonvulsant therapy for status epilepticus

Intravenous immunoglobulin for Guillain-Barré syndrome

Updated Reviews – August 2014

Gamma aminobutyric acid (GABA) receptor agonists for acute stroke

Haemodilution for acute ischaemic stroke

Withdrawn Reviews – August 2014

Treatment for swallowing difficulties (dysphagia) in chronic muscle disease

Journal Articles

Please click on the blue link at the end of the abstract (where available) to access full text. You may need an Athens username and password. To register for an Athens account click here. If you have any difficulty accessing the full text articles, or if you would like us to obtain any of the articles for you, please contact the Healthcare Library.

Table of Contents

Motor Neurone Disease

1. Advances in motor neurone disease

2. Feasibility, acceptability and potential effectiveness of dignity therapy for family carers of people with motor neurone disease

3. Introduction of a close observation unit on a thoracic medicine ward-review of outcomes in the first twelve months
4. Motor neurone disease

5. Narrative analysis of dying with motor neurone disease

6. Non-invasive ventilation during percutaneous endoscopic gastrostomy insertion in motor neurone disease patients – A safe and effective multi-disciplinary approach

7. The genetics of primary progressive aphasia

8. The use of botulinum toxin injections to manage drooling in amyotrophic lateral sclerosis/motor neurone disease: A systematic review

9. Understanding psycho-social processes underpinning engagement with services in motor neurone disease: A qualitative study

**Multiple Sclerosis**

10. Alemtuzumab for the treatment of relapsing-remitting multiple sclerosis: A review of its clinical pharmacology, efficacy and safety

11. Alemtuzumab: the advantages and challenges of a novel therapy in MS

12. Cognitive dysfunction in pediatric multiple sclerosis

13. Dimethyl fumarate: A guide to its use in relapsing-remitting multiple sclerosis

14. Efficacy of vaccination against influenza in patients with multiple sclerosis: The role of concomitant therapies

15. Experimental autoimmune encephalomyelitis is a good model of multiple sclerosis if used wisely


17. Fostering adherence to injectable disease-modifying therapies in multiple sclerosis


19. Menopause in multiple sclerosis: Therapeutic considerations


21. Natalizumab: Risk stratification of individual patients with multiple sclerosis

22. Osteoporosis and multiple sclerosis: Risk factors, pathophysiology, and therapeutic interventions

23. PET imaging in multiple sclerosis

25. Risk stratification and mitigation in multiple sclerosis

26. The link between multiple sclerosis and depression

27. The role of glutamate and its receptors in multiple sclerosis

**Epilepsy**

28. Anesthesia-induced epilepsy: Causes and treatment

29. Calcium signaling and epilepsy

30. Seizure detection, seizure prediction, and closed-loop warning systems in epilepsy

31. Structural connectivity based whole brain modelling in epilepsy

32. The adverse effects profile of levetiracetam in epilepsy: A more detailed look

33. The consequences of refractory epilepsy and its treatment

34. The problem of osteoporosis in epileptic patients taking antiepileptic drugs

35. Vitamin C: A new auxiliary treatment of epilepsy?

36. What happens to children with epilepsy when they become adults? Some facts and opinions

**Parkinson’s Disease**

37. 709-718 Meta-analysis comparing deep brain stimulation of the globus pallidus and subthalamic nucleus to treat advanced Parkinson disease: A review

38. Can stress trigger Parkinson's disease?

39. Correlation between the biochemical pathways altered by mutated parkinson-related genes and chronic exposure to manganese

40. Development of targeted therapies for Parkinson's disease and related synucleinopathies

41. Imaging insights into basal ganglia function, Parkinson's disease, and dystonia

42. Management of Lower Urinary Tract Dysfunction in Parkinson's Disease: A Review of Recent Treatment Options

43. Pharmacogenetic and optical dissection for mechanistic understanding of Parkinson's disease: Potential utilities revealed through behavioural assessment

44. Rasagiline for Parkinson's disease: A meta-analysis
Motor Neurone Disease

1. Advances in motor neurone disease
Citation: Journal of the Royal Society of Medicine, January 2014, vol./is. 107/1(14-21), 0141-0768 (January 2014)
Author(s): Baumer D.; Talbot K.; Turner M.R.
Language: English
Abstract: Motor neurone disease (MND), the commonest clinical presentation of which is amyotrophic lateral sclerosis (ALS), is regarded as the most devastating of adult-onset neurodegenerative disorders. The last decade has seen major improvements in patient care, but also rapid scientific advances, so that rational therapies based on key pathogenic mechanisms now seem plausible. ALS is strikingly heterogeneous in both its presentation, with an average one-year delay from first symptoms to diagnosis, and subsequent rate of clinical progression. Although half of patients succumb within 3-4 years of symptom onset, typically through respiratory failure, a significant minority survives into a second decade. Although an apparently sporadic disorder for most patients, without clear environmental triggers, recent genetic studies have identified disease-causing mutations in genes in several seemingly disparate functional pathways, so that motor neuron degeneration may need to be understood as a common final pathway with a number of upstream causes. This apparent aetiological and clinical heterogeneity suggests that therapeutic studies should include detailed biomarker profiling, and consider genetic as well as clinical stratification. The most common mutation, accounting for 10% of all Western hemisphere ALS, is a hexanucleotide repeat expansion in C9orf72. This and several other genes implicate altered RNA processing and protein degradation pathways in the core of ALS pathogenesis. A major gap remains in understanding how such fundamental processes appear to function without obvious deficit in the decades prior to symptom emergence, and the study of pre-symptomatic gene carriers is an important new initiative. The Royal Society of Medicine.
Publication Type: Journal: Review
Source: EMBASE
Full Text: Available from Journal of the Royal Society of Medicine in No link? Ask Salisbury Healthcare Library - please click here to request article.

2. Feasibility, acceptability and potential effectiveness of dignity therapy for family carers of people with motor neurone disease
Citation: BMC Palliative Care, March 2014, vol./is. 13/1, 1472-684X (19 Mar 2014)
Author(s): Bentley B.; O'Connor M.; Breen L.J.; Kane R.
Abstract: Background: Dignity therapy is a brief psychotherapy that has been shown to enhance the end of life experience. Dignity therapy often involves family carers to support patients weakened by illness and family carers are also the usual recipients of the legacy documents created. No research to date has examined the impact of dignity therapy on family carers at the time of the intervention. This study examined the effects of dignity therapy on family carers of people with motor neurone disease (MND). Methods. This is a cross-sectional study utilizing a one-group pre-test post-test design with 18 family carers of people diagnosed with MND. Outcomes measured caregiver burden, anxiety, depression, and hopefulness. Acceptability was measured with a questionnaire. Feasibility was assessed by examining family carers' involvement in the therapy sessions, time taken to conduct sessions, and any special accommodations or deviations from the dignity therapy protocol. Results: There were no significant pre-test post-test changes on the group level, but there were decreases in anxiety and depression on the individual level. Baseline measures indicate that 50% of family carers had moderate to severe scores for anxiety prior to dignity therapy. MND family carers saw benefits to the person with MND and to themselves after bereavement, but acceptability of dignity therapy at the time of the intervention was mixed with some family carers indicating it was helpful, some indicating it was harmful, and many expressing ambivalence. Dignity therapy involving MND family carers is feasible and the involvement of family carers has minimal impact on the therapy. Conclusion: Dignity therapy is not likely to alleviate caregiver burden in MND family carers, but it may have the ability to decrease or moderate anxiety and depression in distressed MND family carers. Dignity therapy is feasible and generally acceptable to MND family carers. Dignity therapists may provide a better experience for family carers when they are aware of acceptance levels and the quality of partner relationships. Trial registration. ANZCTR Trial Number: ACTRN12611000410954. 2014 Bentley et al.; licensee BioMed Central Ltd.

Publication Type: Journal: Article

Source: EMBASE

Full Text: Available from Springer NHS Pilot 2014 (NESLi2) in BMC Palliative Care; Note: ; Collection notes: Academic-License. Please when asked to pick an institution please pick NHS. Please also note access is from 1997 to date only.
Available from ProQuest in BMC Palliative Care
Available from BioMedCentral in BMC Palliative Care
Available from National Library of Medicine in BMC Palliative Care

3. Introduction of a close observation unit on a thoracic medicine ward-review of outcomes in the first twelve months

Citation: Respirology, April 2014, vol./is. 19/(12), 1323-7799 (April 2014)
Author(s): Stead D.; Douglas J.; Ferguson T.; Yang I.; Reid D.; Parnell B.
Language: English

Abstract: Patient care delivered by 'Nursing Specials' (one on one nursing care) is a costly venture and, in today's fiscal climate, is not sustainable. However, there is still the need to continue to provide safe, quality patient care, to unwell patients requiring close monitoring in the ward setting. The Thoracic Programme at The Prince Charles Hospital provides care for a range of patients with complex co-morbidities including Hypercapnic Respiratory Failure, Motor Neurone Disease, Muscular Dystrophy, and Respiratory Induced Delirium. These patients require one on one nursing when unwell in the ward environment. History: From July 2011 to January 2012, nursing specials in the Thoracic Programme accounted for an expenditure of almost $310 000, equating to 9684 nursing
hours, or an FTE of 4.90 nurses. Aim: To develop an alternative and cost effective model of care to Nursing Specials that would provide safe and effective nursing care to a cohort of patients with severe respiratory problems. Method: A section of a thoracic ward was redeveloped to create a dedicated, purpose built six bed 'Close Observation Unit' (COU), with the aim of providing multi-disciplinary care to a cohort of higher acuity patients. Specific admission criteria were developed to ensure admission of appropriate patients. The existing one to one nursing model was adapted changing to 3 nurses for 6 patients.

Results: From April to September 2013, 298 patients were admitted to the Close Observation Unit, dramatically reducing the number of patients being 'specialled' across the Thoracic Programme. Our experience over the first six months of care provision and patient outcomes on the COU will be presented. Preliminary analyses suggest that there have been significant cost.

Conclusion: Caring for high acuity patients in a close observation setting facilitates safe care that is more cost effective than conventional Nurse Specials and also provides the opportunity for up-skilling of nursing teams involved in the care of unwell patients with severe respiratory illnesses. Data collection is ongoing.

Publication Type: Journal: Conference Abstract
Source: EMBASE
Full Text: Available from Respirology (Carlton, Vic.) in No link? Ask Salisbury Healthcare Library - please click here to request article.

4. Motor neurone disease

Citation: BMJ (Online), July 2014, vol./is. 349/, 1756-1833 (09 Jul 2014)
Author(s): Nageshwaran S.; Davies L.M.; Rafi I.; Radunovic A.
Language: English
Publication Type: Journal: Article
Source: EMBASE
Full Text: Available from Highwire Press in The BMJ
Available from BMJ (Clinical research ed.) in No link? Ask Salisbury Healthcare Library - please click here to request article.

5. Narrative analysis of dying with motor neurone disease

Citation: Palliative Medicine, June 2014, vol./is. 28/6(864), 0269-2163 (June 2014)
Author(s): O'Toole S.; Kemple M.
Language: English
Abstract: The aim of this study was to document the constructions of dying with MND provided by individuals who had witnessed the death of a relative with MND. A narrative approach was used to address the research question: "What are the constructions of dying with MND provided by family members who witnessed the death of a relative with MND?" A combined thematic, structural and performative analysis of narratives was conducted in order to describe the broad patterns within and across the sample and variations within individual narratives. The constructions of dying with MND by those who witnessed the death of a relative with the disease, although characterised by plurality and diversity, were constructions of suffering. These narratives did not reveal accounts of choking or suffocation at the time of death. While almost all of the narratives related to accounts of dying quickly, peacefully and without pain, they were interwoven with experiences of suffering that occurred during the long trajectories of dying related by these research participants. Suffering was theorised as being of both physical and iatrogenic in origin and was related to the intermeshed components of the physical manifestations of MND, the systems of health care, and to the individuals within these systems, upon which the dying person and his or her family were dependent. This study contributed to existing knowledge by focusing on relatives’ narratives of dying and, in doing so, revealed
detailed constructions in which dying with MND was viewed as encompassing the entire
disease trajectory.

Publication Type: Journal: Conference Abstract
Source: EMBASE
Full Text: Available from ProQuest in Palliative Medicine
Available from Palliative medicine in No link? Ask Salisbury Healthcare Library - please click here to request article.

6. Non-invasive ventilation during percutaneous endoscopic gastrostomy insertion in motor
neurone disease patients -
A safe and effective multi-disciplinary approach
Citation: Gut, June 2014, vol./is. 63/(A17-A18), 0017-5749 (June 2014)
Author(s): Smith M.R.; Matsou A.; Nathani N.; Cooney R.
Language: English
Abstract: Introduction Percutaneous endoscopic gastrostomy (PEG) is recommended for motor
neurone disease patients with dysphagia and accelerated weight loss. However PEG has
been suggested as inadvisable in the past in patients with impaired respiratory function.
Recent small studies have found satisfactory outcomes using non invasive ventilation
(NIV) to assist PEG placement in this setting. We set up a service performing this
technique for our region, and analysed our outcomes. Methods 26 patients with motor
neurone disease were included in the study from Nov 2011 - Oct 2013; 11 (42%) were
external referrals. Patients had respiratory assessment prior to the procedure including
sniff nasal pressures, arterial CO2 measurement, overnight oximetry and spirometry as
directed by our respiratory physician. A modified oro-nasal mask with a endoscopic port
was fitted prior to the procedure and NIV initiated and controlled by the respiratory
physician. The PEG (Freka PEG, Bad Homburg, Germany) was inserted under continuous
NIV which continued until the patient was fully awake in recovery. Prophylactic
antibiotics were given routinely. Demographic and technical data, complications and
survival were recorded. Results Median age at time of PEG was 68 yrs (range 43-92),
male 42%. Mean BMI was 22 (range 16-33). 3 patients (12%) were receiving NIV prior
to referral. Mean dose of midazolam was 1.4 mg (range 0-3.5). 2 patients had local
anaesthetic spray as an alternative. PEG tube was successfully placed in 25 (96%)
patients; in 1 the procedure had to be abandoned due to laryngospasm and hypoxia.
Median observed follow up post-PEG insertion was 186 days (range 16-677). There was
1 death within 30 days of PEG placement, at day 16 due to pneumonia superimposed on
type 2 respiratory failure. 19 patients died (73%) during follow up, all due to
complications of the index disease, with median time to death 150 days (range 16-441).
There were minor complications in 3 patients (12%) (2 PEG site infection treated
successfully, 1 respiratory depression requiring flumazenil). Conclusion PEG placement
can be safely and effectively achieved in MND patients with impaired respiratory
function using non invasive ventilatory support. This offers a viable alternative to
radiological or surgical techniques in these patients. We advocate a referral service for
this specialised multi-specialty approach.

Publication Type: Journal: Conference Abstract
Source: EMBASE
Full Text: Available from Gut in No link? Ask Salisbury Healthcare Library - please click here to request article.
Available from Highwire Press in Gut

7. The genetics of primary progressive aphasia
Background: Primary progressive aphasia (PPA) is a disorder in which language impairment is the initial and predominant symptom. Three main phenotypes are described, the nonfluent variant (nfvPPA), the semantic variant (svPPA) and the logopenic variant (lvPPA). Although PPA is most commonly a sporadic disorder, recent studies have shown an association of PPA with mutations in a number of genes.

Aims: To understand the extent to which PPA may be inherited, which genetic mutations may cause it, and whether the phenotypes of genetic PPA differ from sporadic PPA.

Main Contribution: In around 20-30% of patients with PPA, a family history is present although nfvPPA is more heritable than svPPA and lvPPA which are both usually sporadic disorders. Mutations in the progranulin (GRN) and chromosome 9 open reading frame 72 (C9orf72), genes are the major causes of genetic PPA.

Conclusions: Key pointers that may suggest testing for a GRN mutation in PPA are a family history of one of the disorders within the frontotemporal dementia spectrum, a nfvPPA phenotype, particularly if presenting with a prominent anomia and asymmetrical fronto-temporo-parietal atrophy. In someone with nfvPPA and a family history, GRN should be tested initially but a search for hexanucleotide repeat expansions in the C9orf72 gene should be performed if negative, particularly if there are features of motor neurone disease, or a family history of someone with motor neurone disease. Mutations in other genes are only very rare causes of PPA but if GRN and C9orf72 are both negative, testing for mutations in the microtubule-associated protein tau (MAPT), valosin-containing protein (VCP) and presenilin 1 (PSEN1) should be considered.


8. The use of botulinum toxin injections to manage drooling in amyotrophic lateral sclerosis/motor neurone disease: A systematic review

Citation: Dysphagia, August 2014, vol./is. 29/4(500-508), 0179-051X;1432-0460 (August 2014)

Author(s): Squires N.; Humberston M.; Wills A.; Arthur A.

Language: English

Abstract: Difficulty in managing oral secretions is commonly experienced by patients with amyotrophic lateral sclerosis (ALS)/motor neurone disease (MND) and associated bulbar weakness including dysphagia. There are no definitive evidence-based treatment guidelines to manage the distressing symptom of drooling. We reviewed the evidence for the effectiveness of botulinum toxin injections to reduce saliva in ALS/MND. The search strategy was conducted in four stages: (1) electronic search of relevant databases, (2) hand searches of all international ALS/MND symposium journals, (3) email request to MND care centres in the UK and Ireland, and (4) hand searching of reference lists. All studies were critically appraised and relevant data extracted. Botulinum toxin type A and type B were analysed separately. Due to heterogeneity, it was not possible to calculate a pooled estimate of effect. Twelve studies met the inclusion criteria (9 for type A and 3 for type B). Only two randomised controlled trials were identified. Study sample sizes were small with a mean of 12.5 subjects. The most frequently reported outcomes were weight of cotton rolls and number of tissues used. All studies claimed the intervention tested was effective, but only seven studies (4 for type A and 3 for type B) reported statistically significant differences. Although there is evidence to suggest that botulinum toxin B can reduce drooling, the evidence base is limited by a lack of randomized controlled trials.
Evidence to support the use of botulinum toxin A is weaker. Larger trials will help remove the uncertainty practitioners face in treating this disabling symptom. 2014 Springer Science+Business Media.

**Publication Type:** Journal: Article  
**Source:** EMBASE  
**Full Text:** Available from Dysphagia in No link? Ask Salisbury Healthcare Library - please click here to request article.

9. Understanding psycho-social processes underpinning engagement with services in motor neurone disease: A qualitative study  
**Citation:** Palliative Medicine, April 2014, vol./is. 28/4(318-325), 0269-2163;1477-030X (April 2014)  
**Author(s):** Foley G.; Timonen V.; Hardiman O.  
**Language:** English  
**Abstract:** Background: People with motor neurone disease access healthcare services from disease onset to end-of-life care, but there has been paucity of research on how people with motor neurone disease understand and use healthcare services. Aim: To identify key psycho-social processes that underpin how people with motor neurone disease engage with healthcare services. Design: Grounded theory approach comprising in-depth qualitative interviews was used in this study. Data were collected and analysed using open, axial and selective coding procedures. Setting/participants: A total of 34 people with motor neurone disease were recruited from the Irish motor neurone disease population-based register. Results: We identified that control, reassurance, resignation and trust are key variables that shape how people with motor neurone disease engage with healthcare services. Participants exerted control in care to cope with loss. Most participants were resigned to death and sought reassurances from healthcare professionals about end-of-life care. Participants questioned the benefit of lifesustaining interventions in motor neurone disease and few of them associated life-sustaining interventions with palliative care. Participants trusted healthcare professionals who reassured them about their care and who were attuned to how they were coming to terms with loss. Conclusion: This study identified new and important aspects of control, trust and reassurance which shed light on how people with motor neurone disease engage with healthcare professionals and approach end-of-life care. People with motor neurone disease exert control in care and meaningful relationships with healthcare professionals are important to them. Some people with motor neurone disease prefer to die without life-sustaining interventions. The Author(s) 2013.  
**Publication Type:** Journal: Article  
**Source:** EMBASE  
**Full Text:** Available from ProQuest in Palliative Medicine  
Available from Palliative medicine in No link? Ask Salisbury Healthcare Library - please click here to request article.

Multiple Sclerosis

10. Alemtuzumab for the treatment of relapsing-remitting multiple sclerosis: A review of its clinical pharmacology, efficacy and safety  
**Citation:** Expert Review of Clinical Immunology, October 2014, vol./is. 10/10(1281-1291), 1744-666X;1744-8409 (01 Oct 2014)  
**Author(s):** Jones D.E.; Goldman M.D.  
**Language:** English  
**Abstract:** Multiple sclerosis (MS) is an inflammatory condition of the CNS presumably induced by
an environmental trigger(s) in a genetically susceptible individual. Inflammation is prominent and most susceptible to intervention early in MS, so early treatment with disease-modifying therapies is recommended to reduce relapses and new MRI activity (both markers of inflammation) with the goal of delaying disability progression. Unfortunately, the response to the disease-modifying therapies is variable and often falls short of stopping observable disease activity, so the search for more effective agents continues. Alemtuzumab is a monoclonal antibody against CD52 that has exhibited significant efficacy throughout its clinical trial program in MS; uniquely, some of the studies have demonstrated a sustained reduction in disability in MS patients. Countering this impressive efficacy is an associated high risk of autoimmune events (especially thyroid) and concerns for infection or malignancy given prolonged immunosuppression after treatment with alemtuzumab.

Publication Type: Journal: Review
Source: EMBASE
Full Text: Available from ProQuest in Expert Review of Clinical Immunology
Available from Expert review of clinical immunology in No link? Ask Salisbury Healthcare Library - please click here to request article.

11. Alemtuzumab: the advantages and challenges of a novel therapy in MS
Citation: Neurology, July 2014, vol./is. 83/1(87-97), 1526-632X (1 Jul 2014)
Author(s): Menge T.; Stuve O.; Kieseier B.C.; Hartung H.P.
Language: English
Abstract: Our understanding of the pathogenesis of multiple sclerosis has increased considerably, leading to the development of novel therapeutic approaches and compounds. Several agents have undergone clinical testing and have recently received market authorization or are being evaluated for approval. Alemtuzumab is a humanized monoclonal antibody that rapidly depletes CD52+ cells of the lymphoid lineage from peripheral blood, but spares lymphoid precursor cells. Clinical efficacy and safety data from clinical phase II and III trials-all using interferon-beta-1a as active comparator-are summarized and placed in perspective. This review further analyzes the differential reconstitution of T and B cells as a potential mode of action and the pathogenic link to treatment-emergent secondary autoimmune conditions. Given recent positive opinions by regulatory agencies, this new drug will be positioned for the treatment of active relapsing-remitting multiple sclerosis and enlarge our therapeutic armamentarium. 2014 American Academy of Neurology.
Publication Type: Journal: Review
Source: EMBASE
Full Text: Available from Neurology in No link? Ask Salisbury Healthcare Library - please click here to request article.
Available from Ovid in Neurology

12. Cognitive dysfunction in pediatric multiple sclerosis
Citation: Neuropsychiatric Disease and Treatment, July 2014, vol./is. 10/(1385-1392), 1176-6328;1178-2021 (23 Jul 2014)
Author(s): Suppiej A.; Cainelli E.
Language: English
Abstract: Cognitive and neuropsychological impairments are well documented in adult multiple sclerosis (MS). Research has only recently focused on cognitive disabilities in pediatric cases, highlighting some differences between pediatric and adult cases. Impairments in several functions have been reported in children, particularly in relation to attention, processing speed, visual-motor skills, and language. Language seems to be particularly vulnerable in pediatric MS, unlike in adults in whom it is usually preserved. Deficits in
executive functions, which are considered MS-specific in adults, have been inconsistently reported in children. In children, as compared to adults, the relationship between cognitive dysfunctions and the two other main symptoms of MS, fatigue and psychiatric disorders, was poorly explored. Furthermore, data on the correlations of cognitive impairments with clinical and neuroimaging features are scarce in children, and the results are often incongruent; interestingly, involvement of corpus callosum and reduced thalamic volume differentiated patients identified as having a cognitive impairment from those without a cognitive impairment. Further studies about pediatric MS are needed in order to better understand the impact of the disease on brain development and the resulting effect on cognitive functions, particularly with respect to different therapeutic strategies. 2014 Suppiej and Cainelli.

**Publication Type:** Journal: Review

**Source:** EMBASE

**Full Text:** Available from *National Library of Medicine* in *Neuropsychiatric Disease and Treatment*

### 13. Dimethyl fumarate: A guide to its use in relapsing-remitting multiple sclerosis

**Citation:** Drugs and Therapy Perspectives, September 2014, vol./is. 30/9(303-308), 1172-0360;1179-1977 (September 2014)

**Author(s):** Keating G.M.; Burness C.B.; Deeks E.D.

**Language:** English

**Abstract:** Oral dimethyl fumarate (Tecfidera) is a useful addition to the therapeutic options available to treat relapsing-remitting MS (RRMS). In placebo-controlled trials in patients with RMSS, dimethyl fumarate 240 mg twice daily reduced the annualized relapse rate, the proportion of patients with MS relapse at 2 years, and magnetic resonance imaging-assessed disease activity. Dimethyl fumarate was generally well tolerated, with the most commonly occurring adverse events including flushing and gastrointestinal events. According to interim results of a long-term extension study, dimethyl fumarate provides continued efficacy for up to 4 years of treatment, with no new tolerability concerns. 2014 Springer International Publishing.

**Publication Type:** Journal: Review

**Source:** EMBASE

**Full Text:** Available from *Drugs and Therapy Perspectives* in *No link? Ask Salisbury Healthcare Library - please click here to request article.*

### 14. Efficacy of vaccination against influenza in patients with multiple sclerosis: The role of concomitant therapies

**Citation:** Vaccine, August 2014, vol./is. 32/37(4730-4735), 0264-410X;1873-2518 (20 Aug 2014)

**Author(s):** Pellegrino P.; Carnovale C.; Perrone V.; Pozzi M.; Antoniazzi S.; Radice S.; Clementi E.

**Language:** English

**Abstract:** Multiple sclerosis is a chronic progressive demyelinating disease affecting over 2.1 million patients worldwide. Patients affected by MS are exposed to an increased risk of infection from communicable diseases, which may lead to severe disease relapses. Studies have analysed the issue of vaccination of MS-affected patients. These studies, however, deal mostly with safety-related issues documenting that most vaccines have been proven to be safe in MS patients and that vaccination is not associated with an increased risk of relapses. By contrast, evidence on the efficacy is comparatively scant and not yet systematised in a comprehensive picture. This aspect is however important, as both MS and its treatment alter the immune responses, a situation that may be associated with a reduced vaccine efficacy. We have now reviewed the literature and assessed the effects of the therapy for MS on vaccine efficacy; we focused on the vaccine against influenza as
for the other vaccines the information is still too scant. The majority of drugs appear not associated with a reduced response to vaccination against influenza, with the notable exception of mitoxantrone and glatiramer acetate. For a few drugs, among which natalizumab, information is not sufficiently clear and additional studies are needed to draw a definite conclusion. These results highlight the importance to evaluate the efficacy of vaccination in patients treated with immunosuppressant drugs. 2014 Elsevier Ltd.

**Publication Type:** Journal: Review

**Source:** EMBASE

**Full Text:** Available from Vaccine in *No link? Ask Salisbury Healthcare Library - please click here to request article.*

15. **Experimental autoimmune encephalomyelitis is a good model of multiple sclerosis if used wisely**

**Citation:** Multiple Sclerosis and Related Disorders, September 2014, vol./is. 3/5(555-564), 2211-0348;2211-0356 (September 2014)

**Author(s):** Baker D.; Amor S.

**Language:** English

**Abstract:** Although multiple sclerosis is a uniquely human disease, many pathological features can be induced in experimental autoimmune encephalomyelitis (EAE) models following induction of central nervous system-directed autoimmunity. Whilst it is an imperfect set of models, EAE can be used to identify pathogenic mechanisms and therapeutics. However, the failure to translate many treatments from EAE into human benefit has led some to question the validity of the EAE model. Whilst differences in biology between humans and other species may account for this, it is suggested here that the failure to translate may be considerably influenced by human activity. Basic science contributes to failings in aspects of experimental design and over-interpretation of results and lack of transparency and reproducibility of the studies. Importantly issues in trial design by neurologists and other actions of the pharmaceutical industry destine therapeutics to failure and terminate basic science projects. However animal, particularly mechanism-orientated, studies have increasingly identified useful treatments and provided mechanistic ideas on which most hypothesis-led clinical research is based. Without EAE and other animal studies, clinical investigations will continue to be "look-see" exercises, which will most likely provide more misses than hits and will fail the people with MS that they aim to serve. 2014 Elsevier B.V.

**Publication Type:** Journal: Review

**Source:** EMBASE

16. **Fingolimod: A review of its use in relapsing-remitting multiple sclerosis**

**Citation:** Drugs, August 2014, vol./is. 74/12(1411-1433), 0012-6667;1179-1950 (August 2014)

**Author(s):** Sanford M.

**Language:** English

**Abstract:** Fingolimod (Gilenya) is an orally administered disease modifying agent (DMA) for use in relapsing-remitting multiple sclerosis (RRMS). In placebo-controlled trials in patients with RRMS with active disease, fingolimod 0.5 mg/day significantly reduced the annualized relapse rate (ARR) by approximately one-half over 2-year trial periods. It also significantly increased the proportion of patients with no disability progression, reduced deterioration from baseline in the Extended Disability Status Scale score and reduced MRI markers of disease progression (new/newly enlarging brain lesions and percentage change in brain volume). In a 12-month, comparison with intramuscular interferon beta-1a (IFNbeta- 1a) 30 mug/week, the ARR in fingolimod 0.5 mg/day recipients was significantly lower than in IFNbeta-1a recipients by one-half; fingolimod recipients also
had significantly lower MRI markers of disease progression. In extensions to the pivotal clinical trials, fingolimod exposure for up to 4 years was associated with low relapse rates and continuing benefits in terms of disability and disease progression. In clinical trials, adverse events in fingolimod recipients were generally mild to moderate in severity. In the pivotal placebo-controlled trial, serious adverse events occurred in similar proportions of fingolimod 0.5 mg/day and placebo recipients. First-dose bradycardia and atrioventricular block, which are generally asymptomatic, were clinically important adverse events associated with fingolimod in placebo-controlled trials. The risk for serious cardiovascular adverse events at the approved fingolimod dosage appears to be low in patients without pre-existing cardiac conditions. Fingolimod is an efficacious therapy for RRMS that reduces relapses, disability progression, new brain lesions and loss of brain volume. It has an acceptable tolerability profile and provides a useful alternative treatment in patients with RRMS who have responded poorly to other DMAs. 2014 Springer International Publishing.

**Publication Type:** Journal: Review  
**Source:** EMBASE  
**Full Text:** Available from Drugs in No link? Ask Salisbury Healthcare Library - please click here to request article.

### 17. Fostering adherence to injectable disease-modifying therapies in multiple sclerosis

**Citation:** Expert Review of Neurotherapeutics, September 2014, vol./is. 14/9(1029-1042), 1473-7175;1744-8360 (September 2014)  
**Author(s):** Lugaresi A.; Rottoli M.R.; Patti F.  
**Language:** English  
**Abstract:** Multiple sclerosis requires long-term management, often with disease-modifying therapies. Poor medication adherence, especially to injectables, can increase relapse and hospitalisation rates and consume healthcare resources. We discuss adherence definitions and terminology and its prevalence in multiple sclerosis (MS). Typical causes of poor adherence in patients with MS include: insufficient efficacy or tolerability, concurrent disorders, and consequences of MS (e.g., forgetfulness, depression, fatigue and poor motor skills). Ways to improve adherence rates are reviewed, focusing on interdisciplinary healthcare teams, good communication between healthcare workers and patients (and their families), ongoing support and digital tools to promote adherence. We consider open communication and continuing education to be key, and that MS nurses have a pivotal role in ensuring patients’ adherence to MS medicines. Informa UK, Ltd.  
**Publication Type:** Journal: Review  
**Source:** EMBASE  
**Full Text:** Available from Expert review of neurotherapeutics in No link? Ask Salisbury Healthcare Library - please click here to request article.

### 18. Managing treatment fatigue in patients with multiple sclerosis on long-term therapy: The role of multiple sclerosis nurses

**Citation:** Patient Preference and Adherence, August 2014, vol./is. 8/(1093-1099), 1177-889X (19 Aug 2014)  
**Author(s):** Crawford A.; Jewell S.; Mara H.; McCatty L.; Pelfrey R.  
**Language:** English  
**Abstract:** This article discusses the many ways that nurses can address the factors that lead to treatment fatigue in patients with multiple sclerosis (MS) on long-term disease-modifying therapy, ultimately helping to preserve the patient’s health and quality of life. Patients with MS on long-term therapy may suffer from treatment fatigue and poor adherence due
to a variety of different factors, including difficulties with injections, anxiety/depression, financial problems, and inaccurate beliefs about the MS disease process. Because MS nurses have regular interactions with patients, they are ideally situated to help patients cope with these and other factors that may limit adherence. 2014 Crawford et al.

**Publication Type:** Journal: Review  
**Source:** EMBASE  
**Full Text:** Available from *National Library of Medicine* in *Patient preference and adherence*

19. Menopause in multiple sclerosis: Therapeutic considerations  
**Citation:** Journal of Neurology, July 2014, vol./is. 261/7(1257-1268), 0340-5354;1432-1459 (July 2014)  
**Author(s):** Bove R.; Chitnis T.; Houtchens M.  
**Language:** English  
**Abstract:** While the onset of multiple sclerosis (MS) typically occurs during the childbearing years, many women living with MS are of perimenopausal age. There is frequent overlap between menopausal and MS-related symptoms and co-morbidities (e.g. sexual dysfunction, mood disorders and bladder function). Furthermore, some MS symptoms may be exacerbated by perimenopausal changes such as hot flashes or sleep disturbance. The MS neurologist may frequently be the first to become aware of these symptoms and to play a role in monitoring and managing them. In this review, we describe immunological and neurologic changes at menopause as they may impact MS. We then review common symptoms, including fatigue, depression, sexual function, pain and insomnia, and provide both behavioral and pharmacological suggestions for their management. Next, we discuss the need for osteoporosis and cancer screening in perimenopausal women with MS. Finally, we highlight important research gaps, including what effect, if any, the menopausal transition may play on MS disease course as well as the potential modulatory role of hormone replacement therapies. 2013 Springer-Verlag Berlin Heidelberg.  
**Publication Type:** Journal: Review  
**Source:** EMBASE  
**Full Text:** Available from *Journal of neurology* in *No link? Ask Salisbury Healthcare Library* - please click here to request article.

**Citation:** The Lancet Neurology, September 2014, vol./is. 13/9(936-948), 1474-4422;1474-4465 (September 2014)  
**Author(s):** Waldman A.; Ghezzi A.; Bar-Or A.; Mikaeloff Y.; Tardieu M.; Banwell B.  
**Language:** English  
**Abstract:** The clinical features, diagnostic challenges, neuroimaging appearance, therapeutic options, and pathobiological research progress in childhood-and adolescent-onset multiple sclerosis have been informed by many new insights in the past 7 years. National programmes in several countries, collaborative research efforts, and an established international paediatric multiple sclerosis study group have contributed to revised clinical diagnostic definitions, identified clinical features of multiple sclerosis that differ by age of onset, and made recommendations regarding the treatment of paediatric multiple sclerosis. The relative risks conveyed by genetic and environmental factors to paediatric multiple sclerosis have been the subject of several large cohort studies. MRI features have been characterised in terms of qualitative descriptions of lesion distribution and applicability of MRI aspects to multiple sclerosis diagnostic criteria, and quantitative studies have assessed total lesion burden and the effect of the disease on global and
regional brain volume. Humoral-based and cell-based assays have identified antibodies against myelin, potassium-channel proteins, and T-cell profiles that support an adult-like T-cell repertoire and cellular reactivity against myelin in paediatric patients with multiple sclerosis. Finally, the safety and efficacy of standard first-line therapies in paediatric multiple sclerosis populations are now appreciated in more detail, and consensus views on the future conduct and feasibility of phase 3 trials for new drugs have been proposed.

2014 Elsevier Ltd.

Publication Type: Journal: Review
Source: EMBASE
Full Text: Available from Lancet neurology in No link? Ask Salisbury Healthcare Library - please click here to request article.

21. Natalizumab: Risk stratification of individual patients with multiple sclerosis
Citation: CNS Drugs, July 2014, vol./is. 28/7(641-648), 1172-7047;1179-1934 (July 2014)
Author(s): Tur C.; Montalban X.
Language: English
Abstract: At present, three risk factors for the development of progressive multifocal leukoencephalopathy (PML) in natalizumab-treated patients have been identified: the presence of antibodies against JC virus (JCV); the duration of natalizumab treatment, especially if longer than 2 years; and the use of immunosuppressants prior to receiving natalizumab. The most commonly used strategy to assess the individual PML risk includes serum anti-JCV antibody testing. Based on the knowledge on all known risk factors, an algorithm for PML risk stratification has been proposed, where patients with the highest PML risk are those with positive anti-JCV antibodies, treatment duration longer than 2 years, with or without prior history of immunosuppression. These patients would have an approximate incidence of PML of 11.1 (with prior immunosuppression) or 4.6 (without prior immunosuppression) cases per 1,000 patients treated with natalizumab (and treatment duration longer than 2 years). In this review, new data on PML risk factors and possible new strategies for PML risk stratification are discussed. 2014 Springer International Publishing.
Publication Type: Journal: Review
Source: EMBASE

22. Osteoporosis and multiple sclerosis: Risk factors, pathophysiology, and therapeutic interventions
Citation: CNS Drugs, August 2014, vol./is. 28/8(731-742), 1172-7047;1179-1934 (August 2014)
Author(s): Gupta S.; Ahsan I.; Mahfooz N.; Abdelhamid N.; Ramanathan M.; Weinstock-Guttman B.
Language: English
Abstract: Multiple sclerosis (MS) is a chronic inflammatory-demyelinating disease of the nervous system. There has been mounting evidence showing that MS is associated with increased risk of osteoporosis and fractures. The development of osteoporosis in MS patients can be related to the cumulative effects of various factors. This review summarizes the common risk factors and physiologic pathways that play a role in development of osteoporosis in MS patients. Physical inactivity and reduced mechanical load on the bones (offsetting gravity) is likely the major contributing factor for osteoporosis in MS. Additional possible factors leading to reduced bone mass are low vitamin D levels, and use of medications such as glucocorticoids and anticonvulsants. The role of the inflammatory processes related to the underlying disease is considered in the context of the complex bone metabolism. The known effect of different MS disease-modifying therapies on bone health is limited. An algorithm for diagnosis and management of osteoporosis in MS is proposed. 2014 Springer International Publishing Switzerland.
23. PET imaging in multiple sclerosis
Citation: Journal of Neuroimmune Pharmacology, September 2014, vol./is. 9/4(468-482), 1557-1890;1557-1904 (September 2014)
Author(s): De Paula Faria D.; Copray S.; Buchpiguel C.; Dierckx R.; De Vries E.
Language: English
Abstract: Positron emission tomography (PET) is a non-invasive technique for quantitative imaging of biochemical and physiological processes in animals and humans. PET uses probes labeled with a radioactive isotope, called PET tracers, which can bind to or be converted by a specific biological target and thus can be applied to detect and monitor different aspects of diseases. The number of applications of PET imaging in multiple sclerosis is still limited. Clinical studies using PET are basically focused on monitoring changes in glucose metabolism and the presence of activated microglia/macrophages in sclerotic lesions. In preclinical studies, PET imaging of targets for other processes, like demyelination and remyelination, has been investigated and may soon be translated to clinical applications. Moreover, more PET tracers that could be relevant for MS are available now, but have not been studied in this context yet. In this review, we summarize the PET imaging studies performed in multiple sclerosis up to now. In addition, we will identify potential applications of PET imaging of processes or targets that are of interest to MS research, but have yet remained largely unexplored. 2014 Springer Science+Business Media.

Citation: European Neurology, July 2014, vol./is. 72/1-2(72-78), 0014-3022;1421-9913 (July 2014)
Author(s): Mauri-Fabrega L.; Diaz-Sanchez M.; Casado-Chocan J.L.; Ucles-Sanchez A.J.
Language: English
Abstract: Background: The pseudotumoral form of multiple sclerosis (MS) is a rare condition with few descriptions in the literature. It supposes a diagnostic challenge especially when appearing at the onset of disease. Methods: We retrospectively describe a case series of pseudotumoral MS patients that attended our hospital from 2004, analyzing demographic, clinical and radiological variables. We classified the lesions according to the recently proposed morphologic classification (infiltrative, megacystic, Balo or ring-like) and according to the contrast enhancement pattern (nodular, complete ring, incomplete ring and diffuse). Results: Fourteen patients (11 female, 3 male), with a mean age of 35 years, were identified. All of them suffered from a relapsing-remitting form of MS. Eleven patients (78.57%) had symptomatic pseudotumoral lesions (PL), being the form of clinical presentation in the majority of those patients that were symptomatic (81.81%). Several patients presented atypical clinical manifestations such as cognitive impairment (21.42%) and epileptic seizures (14.28%). Full recovery was found in 53.84% of all symptomatic episodes. After a mean follow-up of 43 months, recurrent PL episodes were seldom observed (21.42%), the annualized relapse rate was 0.95 and the mean final Expanded Disability Status Scale score was 1.5. The majority of PLs were supratentorial, coexisted with typical demyelinating plaques and showed the ring-like morphology and the ring pattern of contrast enhancement. Three patients had more than one PL on the
same scan, all of the lesions with similar morphology. Conclusions: Our findings contribute to a better characterization of pseudotumoral forms of MS. However, larger studies are required to define this atypical entity more exactly. 2014 S. Karger AG, Basel.

**Publication Type:** Journal: Review

**Source:** EMBASE

**Full Text:** Available from *European neurology* in *No link? Ask Salisbury Healthcare Library - please click here to request article.*

### 25. Risk stratification and mitigation in multiple sclerosis

**Citation:** Multiple Sclerosis and Related Disorders, September 2014, vol./is. 3/5(639-649), 2211-0348;2211-0356 (September 2014)

**Author(s):** Ontaneda D.; Cohn S.; Fox R.J.

**Language:** English

**Abstract:** The increasing availability of new agents to treat multiple sclerosis poses new challenges for clinicians who seek therapies that are both safe and effective for their patients. The introduction of additional effective therapies has been accompanied by the recognition of serious side effects. The clinician now must weigh both the benefits and risks of therapies to help patients decide which treatment best fits each patient's risk/benefit profile. An optimal selection of therapies relies on a complete understanding of the risks of therapies and the factors that may help evaluate and mitigate those risks. An individualized treatment approach that incorporates patient and disease factors is needed for each patient. In this review, we present risk stratification and mitigation strategies of disease modifying agents for multiple sclerosis. 2014 Elsevier B.V.

**Publication Type:** Journal: Review

**Source:** EMBASE

### 26. The link between multiple sclerosis and depression

**Citation:** Nature Reviews Neurology, September 2014, vol./is. 10/9(507-517), 1759-4758;1759-4766 (29 Sep 2014)

**Author(s):** Feinstein A.; Magalhaes S.; Richard J.-F.; Audet B.; Moore C.

**Language:** English

**Abstract:** Depression - be it a formal diagnosis based on consensus clinical criteria, or a collection of symptoms revealed by a self-report rating scale - is common in patients with multiple sclerosis (MS) and adds substantially to the morbidity and mortality associated with this disease. This Review discusses the prevalence and epidemiology of depression in patients with MS, before covering aetiological factors, including genetics, brain pathology, immunological changes, dysregulation of the hypothalamic-pituitary-adrenal axis, and psychosocial influences. Treatment options such as antidepressant drugs, cognitive-behavioural therapy, mindfulness-based therapy, exercise and electroconvulsive therapy are also reviewed in the context of MS-related depression. Frequent comorbid conditions, namely pain, fatigue, anxiety, cognitive dysfunction and alcohol use, are also summarized. The article then explores three key challenges facing researchers and clinicians: what is the optimal way to define depression in the context of diseases such as MS, in which the psychiatric and neurological symptoms overlap; how can current knowledge about the biological and psychological underpinnings of MS-related depression be used to boost the validity of this construct; and can intervention be made more effective through the use of combination therapies with additive or synergistic effects, which might exceed the modest benefits derived from their individual components?. 2014 Macmillan Publishers Limited. All rights reserved.

**Publication Type:** Journal: Review

**Source:** EMBASE
27. The role of glutamate and its receptors in multiple sclerosis

**Citation:** Journal of Neural Transmission, August 2014, vol./is. 121/8(945-955), 0300-9564;1435-1463 (August 2014)

**Author(s):** Stojanovic I.R.; Kostic M.; Ljubisavljevic S.

**Language:** English

**Abstract:** Glutamate is an excitatory neurotransmitter of the central nervous system, which has a central role in a complex communication network established between neurons, astrocytes, oligodendrocytes, and microglia. Multiple abnormal triggers such as energy deficiency, oxidative stress, mitochondrial dysfunction, and calcium overload can lead to abnormalities in glutamate signaling. Thus, the disturbance of glutamate homeostasis could affect practically all physiological functions and interactions of brain cells, leading to excitotoxicity. Excitotoxicity is the pathological process by which nerve cells are damaged or killed by excessive stimulation by glutamate. Although neuron degeneration and death are the ultimate consequences of multiple sclerosis (MS), it is now widely accepted that alterations in the function of surrounding glial cells are key features in the progression of the disease. The present knowledge raise the possibility that the modulation of glutamate release and transport, as well as receptors blockade or glutamate metabolism modulation, might be relevant targets for the development of future therapeutic interventions in MS. 2014 Springer-Verlag.

**Publication Type:** Journal: Review

**Source:** EMBASE

**Full Text:** Available from Journal of neural transmission in No link? Ask Salisbury Healthcare Library - please click here to request article.

---

**Epilepsy**

28. Anesthesia-induced epilepsy: Causes and treatment

**Citation:** Expert Review of Neurotherapeutics, September 2014, vol./is. 14/9(1099-1113), 1473-7175;1744-8360 (September 2014)

**Author(s):** Zhao X.; Wang X.

**Language:** English

**Abstract:** Epilepsy is a type of chronic brain disease that results from an abnormally high synchronization of neuronal discharge. The typical clinical features of epilepsy are paroxysms and transient and stereotyped brain dysfunction. Many cases of epileptic seizures occurring during anesthesia have been reported. Recently, risk assessment of epileptic seizures during surgery and anesthesia has gained increasing attention. In this review, we systematically summarize the influence of anesthesia on epileptic seizures; the types, durations and frequencies of seizures related to anesthesia; and the epidemiology, prevention, treatment and prognosis of epilepsy. We also explore the possible mechanism of epilepsy and provide guidance for anesthesia during surgeries. Informa UK, Ltd.

**Publication Type:** Journal: Review

**Source:** EMBASE

**Full Text:** Available from Expert review of neurotherapeutics in No link? Ask Salisbury Healthcare Library - please click here to request article.

---

29. Calcium signaling and epilepsy

**Citation:** Cell and Tissue Research, August 2014, vol./is. 357/2(385-393), 0302-766X;1432-0878
Calcium signaling is involved in a multitude of physiological and pathophysiological mechanisms. Over the last decade, it has been increasingly recognized as an important factor in epileptogenesis, and it is becoming obvious that the excess synchronization of neurons that is characteristic for seizures can be linked to various calcium signaling pathways. These include immediate effects on membrane excitability by calcium influx through ion channels as well as delayed mechanisms that act through G-protein coupled pathways. Calcium signaling is able to cause hyperexcitability either by direct modulation of neuronal activity or indirectly through calcium-dependent gliotransmission. Furthermore, feedback mechanisms between mitochondrial calcium signaling and reactive oxygen species are able to cause neuronal cell death and seizures. Unravelling the complexity of calcium signaling in epileptogenesis is a daunting task, but it includes the promise to uncover formerly unknown targets for the development of new antiepileptic drugs.

Seizure detection, seizure prediction, and closed-loop warning systems in epilepsy

Nearly one-third of patients with epilepsy continue to have seizures despite optimal medication management. Systems employed to detect seizures may have the potential to improve outcomes in these patients by allowing more tailored therapies and might, additionally, have a role in accident and SUDEP prevention. Automated seizure detection and prediction require algorithms which employ feature computation and subsequent classification. Over the last few decades, methods have been developed to detect seizures utilizing scalp and intracranial EEG, electrocardiography, accelerometry and motion sensors, electrodermal activity, and audio/video captures. To date, it is unclear which combination of detection technologies yields the best results, and approaches may ultimately need to be individualized. This review presents an overview of seizure detection and related prediction methods and discusses their potential uses in closed-loop warning systems in epilepsy.

Structural connectivity based whole brain modelling in epilepsy

Epilepsy is a neurological condition characterised by the recurrence of seizures. During seizures multiple brain areas can behave abnormally. Rather than considering each
abnormal area in isolation, one can consider them as an interconnected functional ‘network’. Recently, there has been a shift in emphasis to consider epilepsy as a disorder involving more widespread functional brain networks than perhaps was previously thought. The basis for these functional networks is proposed to be the static structural brain network established through the connectivity of the white matter. Additionally, it has also been argued that time varying aspects of epilepsy are of crucial importance and as such computational models of these dynamical properties have recently advanced. We describe how dynamic computer models can be combined with static human in vivo connectivity obtained through diffusion weighted magnetic resonance imaging. We predict that in future the use of these two methods in concert will lead to predictions for optimal surgery and brain stimulation sites for epilepsy and other neurological disorders.

2014 Elsevier B.V.

**Publication Type:** Journal: Review
**Source:** EMBASE
**Full Text:** Available from *Journal of neuroscience methods* in [No link? Ask Salisbury Healthcare Library - please click here to request article.](#)

32. The adverse effects profile of levetiracetam in epilepsy: A more detailed look

**Citation:** International Journal of Neuroscience, September 2014, vol./is. 124/9(627-634), 0020-7454;1563-5279 (September 2014)

**Author(s):** Mbizvo G.K.; Dixon P.; Hutton J.L.; Marson A.G.
**Language:** English
**Abstract:** The adverse effects profile of levetiracetam in epilepsy is still being fully described. We recently published a Cochrane Review evaluating the effectiveness of levetiracetam, added on to usual care, in treating drug-resistant focal epilepsy. The five most common adverse effects were reported and analysed with no scope for reporting any less common adverse effects than those. Here, we report and analyse the remaining adverse effects (including the five most common). These were (in decreasing order of frequency) somnolence; headache; asthenia; accidental injury; dizziness; infection; pharyngitis; pain; rhinitis; abdominal pain; flu syndrome; vomiting; diarrhoea; convulsion; nausea; increased cough; anorexia; upper respiratory tract infection; hostility; personality disorder; urinary tract infection; nervousness; depression; aggression; back pain; agitation; emotional liability; psychomotor hyperactivity; pyrexia; rash; ECG abnormalities; decreased appetite; nasal congestion; irritability; abnormal behaviour; epistaxis; insomnia; altered mood; anxiety; bloody urine; diplopia; dissociation; memory impairment; pruritis; increased appetite; acne; and stomach discomfort. Only somnolence and infection were significantly associated with levetiracetam. When adverse effects pertaining to infection were combined, these affected 19.7% and 15.1% of participants on levetiracetam and placebo (relative risk 1.16, CI 0.89-1.50, Chi<sup>2</sup> heterogeneity p = 0.13). Somnolence and infection further retained significance in adults while no single adverse effect was significant in children. This review updates the adverse effects profile data on levetiracetam use by empirically reporting its common and uncommon adverse effects and analysing their relative importance statistically using data from a group of trials that posses low Risk of Bias and high Quality of Evidence GRADE scores. 2014 Informa Healthcare USA, Inc.

**Publication Type:** Journal: Review
**Source:** EMBASE
**Full Text:** Available from *The International journal of neuroscience* in [No link? Ask Salisbury Healthcare Library - please click here to request article.](#)
33. The consequences of refractory epilepsy and its treatment

**Citation:** Epilepsy and Behavior, August 2014, vol./is. 37/(59-70), 1525-5050;1525-5069 (August 2014)

**Author(s):** Laxer K.D.; Trinka E.; Hirsch L.J.; Cendes F.; Langfitt J.; Delanty N.; Resnick T.; Benbadis S.R.

**Language:** English

**Abstract:** Seizures in some 30% to 40% of patients with epilepsy fail to respond to antiepileptic drugs or other treatments. While much has been made of the risks of new drug therapies, not enough attention has been given to the risks of uncontrolled and progressive epilepsy. This critical review summarizes known risks associated with refractory epilepsy, provides practical clinical recommendations, and indicates areas for future research. Eight international epilepsy experts from Europe, the United States, and South America met on May 4, 2013, to present, review, and discuss relevant concepts, data, and literature on the consequences of refractory epilepsy. While patients with refractory epilepsy represent the minority of the population with epilepsy, they require the overwhelming majority of time, effort, and focus from treating physicians. They also represent the greatest economic and psychosocial burdens. Diagnostic procedures and medical/surgical treatments are not without risks. Overlooked, however, is that these risks are usually smaller than the risks of long-term, uncontrolled seizures. Refractory epilepsy may be progressive, carrying risks of structural damage to the brain and nervous system, comorbidities (osteoarthritis, fractures), and increased mortality (from suicide, accidents, sudden unexpected death in epilepsy, pneumonia, vascular disease), as well as psychological (depression, anxiety), educational, social (stigma, driving), and vocational consequences. Adding to this burden is neuropsychiatric impairment caused by underlying epileptogenic processes ("essential comorbidities"), which appears to be independent of the effects of ongoing seizures themselves. Tolerating persistent seizures or chronic medicinal adverse effects has risks and consequences that often outweigh risks of seemingly "more aggressive" treatments. Future research should focus not only on controlling seizures but also on preventing these consequences. 2014.

**Publication Type:** Journal: Review

**Source:** EMBASE

**Full Text:** Available from Epilepsy & behavior : E&B in No link? Ask Salisbury Healthcare Library - please click here to request article.

34. The problem of osteoporosis in epileptic patients taking antiepileptic drugs

**Citation:** Expert Opinion on Drug Safety, July 2014, vol./is. 13/7(935-946), 1474-0338;1744-764X (July 2014)

**Author(s):** Miziak B.; Blaszczyk B.; Chroscinska-Krawczyk M.; Danilkiewicz G.; Jagiello-Wojtowicz E.; Czuczwar S.J.

**Language:** English

**Abstract:** Introduction: Epilepsy is a common neurological disorder associated with recurrent seizures. Therapy with antiepileptic drugs (AEDs) helps achieve seizure remission in approximately 70% of epileptic patients. Treatment with AEDs is frequently lifelong and there are reports suggesting its negative influence on bone health. This is especially important in terms of general occurrence of osteoporosis, affecting over 50 million people worldwide. Areas covered: This study refers to two main groups of AEDs: hepatic enzyme inducers (carbamazepine, oxcarbazepine, phenobarbital, phenytoin, primidone and topiramate) and non-inducers (clobazam, clonazepam, ethosuximide, gabapentin, lacosamide, lamotrigine, levetiracetam, pregabalin, tiagabine, valproate, vigabatrin and zonisamide). Some reports indicate that enzyme inducers may exert a more negative
influence on bone mineral density (BMD) compared to non-inducers. Bone problems may appear in both sexes during AED therapy, although women are additionally burdened with postmenopausal osteoporosis. Supplementation of vitamin D and calcium in patients on AEDs is recommended. Expert opinion: Apart from enzyme inducers, valproate (an even enzyme inhibitor) may also negatively affect BMD. However, the untoward effects of AEDs may depend upon their doses and duration of treatment. Although the problem of supplementation of vitamin D and calcium in epileptic patients on AEDs is controversial, there are recommendations to do so. 2014 Informa UK, Ltd.

35. Vitamin C: A new auxiliary treatment of epilepsy?

Citation: Pharmacological Reports, August 2014, vol./is. 66/4(529-533), 1734-1140 (August 2014)

Author(s): Sawicka-Glazer E.; Czuczwar S.J.

Language: English

Abstract: Although many approaches to the therapy of epilepsy exist, most of antiepileptic drugs, beside certain and unquestioned benefits, have convinced disadvantages. That is the reason for looking for new methods of treatment. Ascorbic acid, as an antioxidant and electron donor accumulated in central nervous system, seems to take part in diminishing reactions of oxidative stress in brain and cooperate with other antioxidants like alpha-tocopherol. Vitamin C, easily transported through the blood-brain barrier, is proved to reduce injury in the hippocampus during seizures. Depending on type of seizures, it has mostly inhibitory activity and even decreases mortality. Moreover, vitamin C acts as a neuroprotective factor by consolidating cell membranes and decreasing lipid peroxidation. A possible adjunctive role of vitamin C in epileptic patients needs to be considered. 2014 Institute of Pharmacology, Polish Academy of Sciences.

36. What happens to children with epilepsy when they become adults? Some facts and opinions

Citation: Pediatric Neurology, July 2014, vol./is. 51/1(17-23), 0887-8994;1873-5150 (July 2014)

Author(s): Camfield P.R.; Camfield C.S.

Language: English

Abstract: BACKGROUND: The adult outcome after childhood onset epilepsy is a complex subject because seizure types and severity are diverse, comorbidities are common, and additional factors influence social outcome. We review selected data about seizure remission or persistence and social outcome in adulthood. METHODS: Information came from published literature, especially population-based studies. RESULTS: In general, approximately 50-60% of children with epilepsy eventually have complete seizure remission (i.e., seizure free and off antiepileptic drug treatment): with longer follow-up, the remission rate improves. Predicting remission, persistent or intractable epilepsy is often inaccurate for an individual patient. A tiny proportion of children with epilepsy die as the result of seizures or sudden unexpected death in epilepsy patients; however, an otherwise normal child has the same risk of death as the reference population. When uncontrolled epilepsy persists into adulthood, the rate of sudden unexpected death in epilepsy patients possibly increases. Reports about social outcome in adulthood are increasing. For those with intellectual disability, a lifetime of dependency is to be
expected. For those with normal intelligence, adult life is often unsatisfactory with high rates of incomplete education, unemployment, poverty, social isolation, inadvertent pregnancy, and psychiatric disorders. Seizure remission does not ensure good adult social outcome. CONCLUSIONS: Although seizure control in childhood is important, anticipating poor social outcome in adulthood may allow earlier interventions. A well-orchestrated transition from pediatric to adult health care may be beneficial for the 40-50% with persistent seizures and for the majority who are at risk for adult social difficulties. 2014 Elsevier Inc. All rights reserved.

**Publication Type:** Journal: Review  
**Source:** EMBASE  
**Full Text:** Available from Pediatric neurology in No link? Ask Salisbury Healthcare Library - please click here to request article.

### Parkinson's Disease

37. 709-718 Meta-analysis comparing deep brain stimulation of the globus pallidus and subthalamic nucleus to treat advanced Parkinson disease: A review  
**Citation:** Journal of Neurosurgery, September 2014, vol./is. 121/3(709-718), 0022-3085;1933-0693 (September 2014)  
**Author(s):** Liu Y.; Li W.; Tan C.; Liu X.; Wang X.; Gui Y.; Qin L.; Deng F.; Hu C.; Chen L.  
**Language:** English  
**Abstract:** Object. Deep brain stimulation (DBS) is the surgical procedure of choice for patients with advanced Parkinson disease (PD). The globus pallidus internus (GPI) and the subthalamic nucleus (STN) are commonly targeted by this procedure. The purpose of this meta-analysis was to compare the efficacy of DBS in each region. Methods. MEDLINE/PubMed, EMBASE, Web of Knowledge, and the Cochrane Library were searched for English-language studies published before April 2013. Results of studies investigating the efficacy and clinical outcomes of DBS of the GPI and STN for PD were analyzed. Results. Six eligible trials containing a total of 563 patients were included in the analysis. Deep brain stimulation of the GPI or STN equally improved motor function, measured by the Unified Parkinson's Disease Rating Scale Section III (UPDRSIII) (motor section, for patients in on- and off-medication phases), within 1 year postsurgery. The change score for the on-medication phase was 0.68 (95% CI -2.12 to 3.47, p > 0.05; 5 studies, 518 patients) and for the off-medication phase was 1.83 (95% CI -3.12 to 6.77, p > 0.05; 5 studies, 518 patients). The UPDRS Section II (activities of daily living) scores for patients on medication improved equally in both DBS groups (p = 0.97). STN DBS allowed medication dosages to be reduced more than GPI DBS (95% CI 129.27-316.64, p < 0.00001; 5 studies, 540 patients). Psychiatric symptoms, measured by Beck Depression Inventory, 2nd edition scores, showed greater improvement from baseline after GPI DBS than after STN DBS (standardized mean difference -2.28, 95% CI -3.73 to -0.84, p = 0.002; 3 studies, 382 patients). Conclusions. GPI and STN DBS improve motor function and activities of daily living for PD patients. Differences in therapeutic efficacy for PD were not observed between the 2 procedures. STN DBS allowed greater reduction in medication for patients, whereas GPI DBS provided greater relief from psychiatric symptoms. An understanding of other symptomatic aspects of targeting each region and long-term observations on therapeutic effects are needed. AANS, 2014.  
**Publication Type:** Journal: Review  
**Source:** EMBASE  
**Full Text:** Available from Journal of neurosurgery in No link? Ask Salisbury Healthcare Library - please click here to request article.
38. Can stress trigger Parkinson's disease?

**Citation:** Journal of neurology, neurosurgery, and psychiatry, August 2014, vol./is. 85/8(878-881), 1468-330X (Aug 2014)

**Author(s):** Djamshidian A.; Lees A.J.

**Language:** English

**Abstract:** In this manuscript we summarize the role of chronic stress as a potential trigger factor for Parkinson's disease. Underlying mechanisms and stress-induced changes to the neuronal networks have been highlighted. Examples of stress induced reversible symptoms that resemble parkinsonism in humans and in animal models raise the question whether emotional stress can cause striatal degeneration in susceptible patients. A Pubmed literature review searching for the terms 'Stress', 'Distress and Parkinson's disease', 'Emotional Distress and Parkinson's disease', 'Stress and Parkinson's disease', 'Prodromal Parkinson's disease', 'Non motor symptoms and Parkinson's disease', 'Paradoxical kinesia', 'Psychogenic parkinsonism', 'Functional somatic syndromes', 'Chronic fatigue syndrome', 'Irritable bowel syndrome', 'Fibromyalgia', 'Dopamine and fibromyalgia', 'Dopamine and chronic fatigue syndrome' and 'Dopamine and irritable bowel syndrome' was carried out until April 2013. Articles were also identified through searches of the authors' own files. Only papers published in English were reviewed. The final reference list was generated on the basis of originality and relevance to the broad scope of this viewpoint. Published by the BMJ Publishing Group Limited. For permission to use (where not already granted under a licence) please go to http://group.bmj.com/group/rights-licensing/permissions.

**Publication Type:** Journal: Review

**Source:** EMBASE

**Full Text:** Available from Highwire Press in *Journal of neurology, neurosurgery, and psychiatry*

39. Correlation between the biochemical pathways altered by mutated parkinson-related genes and chronic exposure to manganese

**Citation:** NeuroToxicology, September 2014, vol./is. 44/(314-325), 0161-813X;1872-9711 (September 2014)

**Author(s):** Roth J.A.

**Language:** English

**Abstract:** The studies presented in this review attempt to describe the operative properties of the genes involved in generation of early and late onset of Parkinson's disease or Parkinson-like disorders and how mutation in these genes relate to onset of manganism. These include the genes alpha-synuclein, parkin, PINK1, DJ-1, ATP13A2, and SLC30A10 which are associated with early-onset of Parkinson's as well as those genes linked with late onset of the disorder which include, LRRK2 and VPS35. Since mutations in these genes and excess Mn potentially disrupt similar cellular processes within the basal ganglia, it is reasonable to hypothesize that the expressed symptoms of Parkinson's disease may overlap with that of manganese (Mn) toxicity. There appears to be four common processes linking the two disorders, as mutations in genes associated with Parkinsonism initiate similar adverse biological reactions acknowledged to stimulate Mn-induced dopaminergic cell death including; (1) disruption of mitochondrial function leading to oxidative stress, (2) abnormalities in vesicle processing, (3) altered proteasomal and lysosomal protein degradation, and (4) alpha-synuclein aggregation The mutual neurotoxic processes provoked by mutations in these genes in concert with the biological disturbances produced by Mn, most likely, act in synchrony to contribute to the severity, characteristics and onset of both disorders. 2014.

**Publication Type:** Journal: Review

**Source:** EMBASE
40. Development of targeted therapies for Parkinson's disease and related synucleinopathies

Citation: Journal of Lipid Research, October 2014, vol./is. 55/10(1996-2003), 0022-2275;1539-7262 (01 Oct 2014)

Author(s): Sybertz E.; Krainc D.

Language: English

Abstract: Therapeutic efforts in neurodegenerative diseases have been very challenging, particularly due to a lack of validated and mechanism-based therapeutic targets and biomarkers. The basic idea underlying the novel therapeutic approaches reviewed here is that by exploring the molecular basis of neurodegeneration in a rare lysosomal disease such as Gaucher's disease (GD), new molecular targets will be identified for therapeutic development in common synucleinopathies. Accumulation of alpha-synuclein plays a key role in the pathogenesis of Parkinson's disease (PD) and other synucleinopathies, suggesting that improved clearance of alpha-synuclein may be of therapeutic benefit. To achieve this goal, it is important to identify specific mechanisms and targets involved in the clearance of alpha-synuclein. Recent discovery of clinical, genetic, and pathological linkage between GD and PD offers a unique opportunity to examine lysosomal glucocerebrosidase, an enzyme mutated in GD, for development of targeted therapies in synucleinopathies. While modulation of glucocerebrosidase and glycolipid metabolism offers a viable approach to treating disorders associated with synuclein accumulation, the compounds described to date either lack the ability to penetrate the CNS or have off-target effects that may counteract or limit their capabilities to mediate the desired pharmacological action. However, recent emergence of selective inhibitors of glycosphingolipid biosynthesis and noninhibitory pharmacological chaperones of glycosphingolipid processing enzymes that gain access to the CNS provide a novel approach that may overcome some of the limitations of compounds reported to date. These new strategies may allow for development of targeted treatments for synucleinopathies that affect both children and adults.

Publication Type: Journal: Review

Source: EMBASE

Full Text: Available from Journal of lipid research in No link? Ask Salisbury Healthcare Library - please click here to request article.

41. Imaging insights into basal ganglia function, Parkinson's disease, and dystonia

Citation: The Lancet, August 2014, vol./is. 384/9942(532-544), 0140-6736;1474-547X (August 9-15, 2014)

Author(s): Stoessl A.J.; Lehericy S.; Strafella A.P.

Language: English

Abstract: Summary Recent advances in structural and functional imaging have greatly improved our ability to assess normal functions of the basal ganglia, diagnose parkinsonian syndromes, understand the pathophysiology of parkinsonism and other movement disorders, and detect and monitor disease progression. Radionuclide imaging is the best way to detect and monitor dopamine deficiency, and will probably continue to be the best biomarker for assessment of the effects of disease-modifying therapies. However, advances in magnetic resonance enable the separation of patients with Parkinson's disease from healthy controls, and show great promise for differentiation between Parkinson's disease and other akinetic-rigid syndromes. Radionuclide imaging is useful to show the dopaminergic basis for both motor and behavioural complications of Parkinson's disease.
and its treatment, and alterations in non-dopaminergic systems. Both PET and MRI can be used to study patterns of functional connectivity in the brain, which is disrupted in Parkinson’s disease and in association with its complications, and in other basal-ganglia disorders such as dystonia, in which an anatomical substrate is not otherwise apparent. Functional imaging is increasingly used to assess underlying pathological processes such as neuroinflammation and abnormal protein deposition. This imaging is another promising approach to assess the effects of treatments designed to slow disease progression. 2014 Elsevier Ltd.

**Publication Type:** Journal: Review
**Source:** EMBASE

**Full Text:** Available from ProQuest in *Lancet, The*
Available from LANCET in *Salisbury District Hospital Healthcare Library*
Available from *The Lancet* in *Lancet, The*
Available from *Lancet* in *No link? Ask Salisbury Healthcare Library - please click here to request article.*

**42. Management of Lower Urinary Tract Dysfunction in Parkinson's Disease: A Review of Recent Treatment Options**

**Citation:** Current Bladder Dysfunction Reports, September 2014, vol./is. 9/3(214-220), 1931-7212;1931-7220 (September 2014)

**Author(s):** Lurvey R.; Duffy A.; Rothschild J.

**Language:** English

**Abstract:** In addition to the cardinal symptoms of tremors and rigidity, Parkinson’s disease is also defined by lower urinary tract dysfunction. In particular, these symptoms of nocturia and detrusor overactivity greatly impact the quality of life of a Parkinson’s patient. Improved understanding of the differential diagnosis of Parkinson’s disease and other neurodegenerative diseases, combined with improvements in treatment for detrusor overactivity, has improved the therapeutic options for Parkinson's disease-associated lower urinary tract dysfunction. In this review, we discuss the various therapeutic options now available. 2014 Springer Science+Business Media New York.

**Publication Type:** Journal: Review
**Source:** EMBASE

**43. Pharmacogenetic and optical dissection for mechanistic understanding of Parkinson's disease: Potential utilities revealed through behavioural assessment**

**Citation:** Neuroscience and Biobehavioral Reviews, November 2014, vol./is. 47/(87-100), 0149-7634;1873-7528 (November 2014)

**Author(s):** Sharma P.; Pienaar I.S.

**Language:** English

**Abstract:** The technology toolbox by which neural elements can be selectively manipulated in vertebrate and invertebrate brains has expanded greatly in recent years, to now include sophisticated optogenetics and novel designer receptors. Application of such tools allow for ascertaining whether a particular behavioural phenotype associates with interrogation of a specific neural circuit. Optogenetics has already found application in the study of Parkinson’s disease (PD) circuitry and therapies, whereas novel designer receptors hold promise for enlightening on current understanding of the mechanisms underlying parkinsonian motor and non-motor symptoms. In particular, this new generation of research tools provide a method by which significant insights can be gained on brain networks implicated in brain diseases such as PD. These tools also promise to assist in the development of novel therapies for targeting degenerated dopaminergic and non-dopaminergic neurons in the diseased basal ganglia system of PD patients, for
providing symptomatic relief or even reverse neurodegenerative processes. The present review discusses how such technologies, in conjunction with application of sensitive behavioural assays, continue to significantly advance our knowledge of circuit and signalling properties inherent to PD pathology. The discussion also highlights how such experimental approaches provide additional explorative avenues which may result in dramatically improved therapeutic options for PD patients. 2014 Elsevier Ltd.

**Publication Type:** Journal: Review

**Source:** EMBASE

### 44. Rasagiline for Parkinson's disease: A meta-analysis

**Citation:** Chinese Journal of Evidence-Based Medicine, 2014, vol./is. 14/2(205-210), 1672-2531 (2014)

**Author(s):** Tong Y.-S.; Yang X.-L.

**Language:** Chinese

**Abstract:** Objective: To systematically review the effectiveness and safety of rasagiline for Parkinson's disease. Methods: Databases including The Cochrane Library (Issue 3, 2013), Web of Science, MEDLINE (Ovid), PubMed, CBM, CNKI, WanFang Data and VIP were electronically searched from inception to March 2013 for randomized controlled trials (RCTs) on rasagiline for Parkinson's disease. Two reviewers independently screened literature according to the inclusion and exclusion criteria, extracted the data, and assessed the methodological quality of included studies. Meta-analysis was performed using RevMan 5.1 software. Results: In total, 6 studies involving 2865 patients were included. The results of meta-analyses indicated that, compared with placebo, rasagiline 2 mg/d and 1 mg/d was significantly effective (MD= -3.16, 95%CI -3.21 to -3.11, P<0.00001; MD= -3.01, 95%CI -3.06 to -2.96, P<0.0001). Rasagiline 1 mg/d was more effective than rasagiline 2 mg/d in the treatment of early PD (MD= -0.65, 95%CI -0.73 to -0.57, P<0.0001). There was no significant difference between rasagiline and placebo in the incidences of nausea, headache, and dizziness (nausea: OR=0.72, 95%CI 0.49 to 1.07, P=0.60; headache: OR=1.02, 95%CI 0.70 to 1.49, P=0.91; dizziness: OR=0.87, 95%CI 0.49 to 1.55, P=0.35). Conclusion: Rasagiline is effective for early Parkinson's disease, and the dosage 1 mg/d is better than 2 mg/d based on current limited evidence. Rasagiline has a good tolerability and safety. Due to the limited quantity of the included studies and the evidence with limited strength, further high-quality RCTs are needed to verify the aforementioned conclusion. 2014 Editorial Board of Chin J Evid-based Med.

**Publication Type:** Journal: Review

**Source:** EMBASE

**Full Text:** Available from *Chinese Journal of Evidence-Based Medicine* in *No link? Ask Salisbury Healthcare Library - please click here to request article.*

### 45. Sex differences in Parkinson's disease and other movement disorders

**Citation:** Experimental neurology, September 2014, vol./is. 259/(44-56), 1090-2430 (Sep 2014)

**Author(s):** Smith K.M.; Dahodwala N.

**Language:** English

**Abstract:** Movement disorders including Parkinson's disease (PD), Huntington's disease (HD), chorea, tics, and Tourette's syndrome (TS) display sex differences in disease susceptibility, disease pathogenesis, and clinical presentation. PD is more common in males than in females. Epidemiologic studies suggest that exposure to endogenous and exogenous estrogen contributes to these sex differences. There is extensive evidence that estrogen prevents dopaminergic neuron depletion induced by neurotoxins in PD animal models and therefore is neuroprotective. Estrogen may also decrease the efficacy of other neuroprotective substances such as caffeine in females but not males. Sex chromosomes
can exert effects independent of sex steroid hormones on the development and maintenance of the dopamine system. As a result of hormone, chromosome and other unknown effects, there are sexual dimorphisms in the basal ganglia, and at the molecular levels in dopaminergic neurons that may lead to distinct mechanisms of pathogenesis in males and females. In this review, we summarize the evidence that estrogen and selective estrogen receptor modulators are neuroprotective in PD and discuss potential mechanisms of action. We also briefly review how sex differences in basal ganglia function and dopaminergic pathways may impact HD, chorea, and tics/Tourette’s syndrome. Further understanding of these sex differences may lead to novel therapeutic strategies for prevention and treatment of these diseases. Copyright 2014 Elsevier Inc. All rights reserved.

Publication Type: Journal: Review
Source: EMBASE
Full Text: Available from Experimental neurology in No link? Ask Salisbury Healthcare Library - please click here to request article.
Available from Elsevier in Experimental Neurology; Note: ; Collection notes: Academic-License. Please note search only titles within the trial dates: 2010 - to-date

46. Slowing of neurodegeneration in Parkinson's disease and Huntington's disease: Future therapeutic perspectives
Citation: The Lancet, August 2014, vol./is. 384/9942(545-555), 0140-6736;1474-547X (August 9-15, 2014)
Author(s): Schapira A.H.V.; Olanow C.W.; Greenamyre J.T.; Bezard E.
Language: English
Abstract: Summary Several important advances have been made in our understanding of the pathways that lead to cell dysfunction and death in Parkinson's disease and Huntington's disease. These advances have been informed by both direct analysis of the post-mortem brain and by study of the biological consequences of the genetic causes of these diseases. Some of the pathways that have been implicated so far include mitochondrial dysfunction, oxidative stress, kinase pathways, calcium dysregulation, inflammation, protein handling, and prion-like processes. Intriguingly, these pathways seem to be important in the pathogenesis of both diseases and have led to the identification of molecular targets for candidate interventions designed to slow or reverse their course. We review some recent advances that underlie putative therapies for neuroprotection in Parkinson's disease and Huntington's disease, and potential targets that might be exploited in the future. Although we will need to overcome important hurdles, especially in terms of clinical trial design, we propose several target pathways that merit further study. In Parkinson's disease, these targets include agents that might improve mitochondrial function or increase degradation of defective mitochondria, kinase inhibitors, calcium channel blockers, and approaches that interfere with the misfolding, templating, and transmission of alpha-synuclein. In Huntington's disease, strategies might also be directed at mitochondrial bioenergetics and turnover, the prevention of protein dysregulation, disruption of the interaction between huntingtin and p53 or huntingtin-interacting protein 1 to reduce apoptosis, and interference with expression of mutant huntingtin at both the nucleic acid and protein levels. 2014 Elsevier Ltd.
Publication Type: Journal: Review
Source: EMBASE
Full Text: Available from ProQuest in Lancet, The
Available from LANCET in Salisbury District Hospital Healthcare Library
Available from The Lancet in Lancet, The
Available from Lancet in No link? Ask Salisbury Healthcare Library - please click here to
47. The association between the LRRK2 G2385R variant and the risk of Parkinson’s disease: A meta-analysis based on 23 case-control studies

Citation: Neurological Sciences, October 2014, vol./is. 35/10(1495-1504), 1590-1874;1590-3478 (01 Oct 2014)


Language: English

Abstract: Clinical diagnosis of Parkinson’s disease (PD) is essential but misdiagnosis of PD-like diseases is quite common. LRRK2 G2385R variants have been extensively examined for the association to the risk of Parkinson’s disease. However, results from different studies are inconsistent. The purpose of this meta-analysis was to assess the association between the LRRK2 G2385R variants and the risk of PD. A systematic literature search was performed for 6 databases up to January of 2014 to identify case-control studies involving LRRK2 G2385R variants and the risk of PD. A total of 12,915 cases and 12,451 controls in 23 case-control studies were included in this meta-analysis. The results indicated that the variant A allele carriers (GA + AA) increased risk of PD when compared with the homozygote GG (GA + AA vs. GG: OR = 2.4, 95% CI = 1.97 to 2.92, P < 0.00001). In the subgroup analysis by ethnicity, increased risks were identified among Chinese (OR = 2.69, 95% CI = 2.1-3.45, P < 0.00001) as well as in non-Chinese (OR = 2.17, 95% CI 1.75-2.69, P < 0.00001). In the subgroup analysis by age of onset, significant associations were found in both later-onset PD (LOPD) and early-onset PD (EOPD) cases. And there was no significant difference of the allele frequency between patients with LOPD and EOPD (OR = 1.18, 95% CI = 0.77-1.80, P = 0.45). Our results suggest that the LRRK2 G2385R variants contribute to the susceptibility of PD especially in Chinese PD. Meanwhile, it is possible that age is not the risk factor to facilitate G2385R gene mutation.

Publication Type: Journal: Review

Source: EMBASE

48. The benefits of pramipexole selection in the treatment of Parkinson’s disease

Citation: Neurological Sciences, October 2014, vol./is. 35/10(1505-1511), 1590-1874;1590-3478 (01 Oct 2014)

Author(s): Silindir M.; Ozer A.Y.

Language: English

Abstract: Levodopa administration as a gold standard in Parkinson’s disease (PD) treatment is very valuable, however, long-term administration may cause some motor complications such as abnormal unintended movements and shortening response to each dose (wearing off phenomenon). Dopamine agonists were developed to reduce duration of immobile off periods and dependence to levodopa for improving motor impairments (Clarke et al., Cochrane Libr 1:1-23, 2000). Pramipexole is one of these nonergot dopamine agonists with high relative in vitro specificity and full intrinsic activity at D2 subfamily of dopamine receptors, with a higher binding affinity to D3 than to D4 or D2 receptor subtypes (Piercey, Clin Neuropharmacol 21:141-151, 1998). It can be advantageously administered as monotherapy or adjunctive therapy to levodopa to decrease side effects and increase effectiveness in both early and advanced PD treatment.

Publication Type: Journal: Review

Source: EMBASE

49. Therapeutic potential of targeting glutamate receptors in Parkinson’s disease

Citation: Journal of Neural Transmission, August 2014, vol./is. 121/8(861-880),
Abstract: Glutamate plays a complex role in many aspects of Parkinson's disease including the loss of dopaminergic neurons, the classical motor symptoms as well as associated non-motor symptoms and the treatment-related side effect, L-DOPA-induced dyskinesia. This widespread involvement opens up possibilities for glutamate-based therapies to provide a more rounded approach to treatment than is afforded by current dopamine replacement therapies. Beneficial effects of blocking postsynaptic glutamate transmission have already been noted in a range of preclinical studies using antagonists of NMDA receptors or negative allosteric modulators of metabotropic glutamate receptor 5 (mGlu5), while positive allosteric modulators of mGlu4 in particular, although at an earlier stage of investigation, also look promising. This review addresses each of the key features of Parkinson's disease in turn, summarising the contribution glutamate makes to that feature and presenting an up-to-date account of the potential for drugs acting at ionotropic or metabotropic glutamate receptors to provide relief. Whilst only a handful of these have progressed to clinical trials to date, notably NMDA and NR2B antagonists against motor symptoms and L-DOPA-induced dyskinesia, with mGlu5 negative allosteric modulators also against L-DOPA-induced dyskinesia, the mainly positive outcomes of these trials, coupled with supportive preclinical data for other strategies in animal models of Parkinson's disease and L-DOPA-induced dyskinesia, raise cautious optimism that a glutamate-based therapeutic approach will have significant impact on the treatment of Parkinson's disease. 2014 Springer-Verlag.

Publication Type: Journal: Review
Source: EMBASE

Full Text: Available from Journal of neural transmission in No link? Ask Salisbury Healthcare Library - please click here to request article.

50. VMAT2 and Parkinson's disease: Harnessing the dopamine vesicle
Citation: Expert Review of Neurotherapeutics, October 2014, vol./is. 14/10(1115-1117), 1473-7175;1744-8360 (01 Oct 2014)
Author(s): Lohr K.M.; Miller G.W.
Language: English
Abstract: Despite a movement away from dopamine-focused Parkinson's disease (PD) research, a recent surge of evidence now suggests that altered vesicular storage of dopamine may contribute to the demise of the nigral neurons in this disease. Human studies demonstrate that the vesicular monoamine transporter 2 (VMAT2; SLC18A2) is dysfunctional in PD brain. Moreover, studies with transgenic mice suggest that there is an untapped reserve capacity of the dopamine vesicle that could be unbridled by increasing VMAT2 function. Therapeutic manipulation of VMAT2 level or function has the potential to improve efficacy of dopamine derived from administered levodopa, increase dopamine neurotransmission from remaining midbrain dopamine neurons and protect against neurotoxic insults. Thus, the development of drugs to enhance the storage of release of dopamine may be a fruitful avenue of research for PD.
Publication Type: Journal: Review
Source: EMBASE
New Library Resources

New Books

New books available from the Healthcare Library.
To search the library catalogue visit www.swims.nhs.uk

Neurological Examination Made Easy
Geraint Fuller
Shelfmark: WL250
Barcode: T026615

Disclaimer and Feedback

This current awareness bulletin contains a selection of information which is not intended to be exhaustive, and although library staff have made every effort to link only to reputable and reliable websites, the information contained in this bulletin has not been critically appraised by library staff. It is therefore the responsibility of the reader to appraise this information for accuracy and relevance.

This bulletin was produced by Helen Clemow, Librarian, Salisbury NHS Foundation Trust Healthcare Library. If you have any comments to make about this bulletin please contact helen.clemow@salisbury.nhs.uk.