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**Epilepsy Abstracts**

1. Commentary: It's time to talk about SUDEP

Citation: Epilepsia, October 2014, vol./is. 55/10(1501-1503), 0013-9580;1528-1167 (01 Oct 2014)
Author(s): Donner E., Buchhalter J.
Language: English
Abstract: Summary Sudden unexpected death in epilepsy (SUDEP) is the most tragic potential outcome of epilepsy. Despite recommendations from epilepsy organizations in the United Kingdom and the United States,
many neurologists choose not to discuss the risk of SUDEP with their patients with epilepsy. Yet, the literature clearly demonstrates that people with epilepsy and their caregivers want to know more about SUDEP. When health care providers do not provide information, people with epilepsy turn to other sources, risking misinformation and potentially increasing anxiety and distress. Sharing accurate information about SUDEP can optimize epilepsy self-management and engage the person with epilepsy as a partner in their own care. Information about SUDEP must be part of the comprehensive education given to all people with epilepsy.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Epilepsia at No link? Ask Salisbury Healthcare Library - please click here to request article.

2. Complex metabolically demanding sensory processing in the olfactory system: Implications for epilepsy

Citation: Epilepsy and Behavior, September 2014, vol./is. 38/(37-42), 1525-5050;1525-5069 (September 01, 2014)
Author(s): Restrepo D., Hellier J.L., Salcedo E.
Language: English
Abstract: Although the olfactory system is not generally associated with seizures, sharp application of odor eliciting activity in a large number of olfactory sensory neurons (OSNs) has been shown to elicit seizures. This is most likely due to increased ictal activity in the anterior piriform cortex-an area of the olfactory system that has limited GABAergic interneuron inhibition of pyramidal output cell activity. Such hyperexcitability in a well-characterized and highly accessible system makes olfaction a potentially powerful model system to examine epileptogenesis. This article is part of a Special Issue entitled "NEWroscience 2013".

Publication type: Journal: Review
Source: EMBASE
Full text: Available Epilepsy & behavior : E&B at No link? Ask Salisbury Healthcare Library - please click here to request article.

3. Early life stress in epilepsy: A seizure precipitant and risk factor for epileptogenesis

Citation: Epilepsy and Behavior, September 2014, vol./is. 38/(160-171), 1525-5050;1525-5069 (September 01, 2014)
Author(s): van Campen J.S., Jansen F.E., de Graan P.N.E., Braun K.P.J., Joels M.
Language: English
Abstract: Stress can influence epilepsy in multiple ways. A relation between stress and seizures is often experienced by patients with epilepsy. Numerous questionnaire and diary studies have shown that stress is the most often reported seizure-precipitating factor in epilepsy. Acute stress can provoke epileptic seizures, and chronic stress increases seizure frequency. In addition to its effects on seizure susceptibility in patients with epilepsy, stress might also increase the risk of epilepsy development, especially when the stressors are severe, prolonged, or experienced early in life. Although the latter has not been fully resolved in humans, various preclinical epilepsy models have shown increased seizure susceptibility in naive rodents after prenatal and early postnatal stress exposure. In the current review, we first provide an overview of the effects of stress on the brain. Thereafter, we discuss human as well as preclinical studies evaluating the relation between stress, epileptic seizures, and epileptogenesis, focusing on the epileptogenic effects of early life stress. Increased knowledge on the interaction between early life stress, seizures, and epileptogenesis could improve patient care and provide a basis for new treatment strategies for epilepsy. This article is part of a Special Issue entitled "NEWroscience 2013"

Publication type: Journal: Review
Source: EMBASE
Full text: Available Epilepsy & behavior : E&B at No link? Ask Salisbury Healthcare Library - please click here to request article.

4. Epileptic seizures as a manifestation of cow's milk allergy: A studied relationship and description of our pediatric experience

Citation: Expert Review of Clinical Immunology, December 2014, vol./is. 10/12(1597-1609), 1744-666X;1744-8409 (01 Dec 2014)
Author(s): Falsaperla R., Pavone P., Sopo S.M., Mahmood F., Scalia F., Corsello G., Lubrano R., Vitaliti G.
Language: English
Abstract: Adverse reactions after ingestion of cow's milk proteins can occur at any age, from birth and even
amongst exclusively breast-fed infants, although not all of these are hypersensitivity reactions. The most common presentations related to cow’s milk protein allergy are skin reactions, failure to thrive, anaphylaxis as well as gastrointestinal and respiratory disorders. In addition, several cases of cow's milk protein allergy in the literature have documented neurological involvement, manifesting with convulsive seizures in children. This may be due to CNS spread of a peripheral inflammatory response. Furthermore, there is evidence that pro-inflammatory cytokines are responsible for disrupting the blood-brain barrier, causing focal CNS inflammation thereby triggering seizures, although further studies are needed to clarify the pathogenic relationship between atopy and its neurological manifestations. This review aims to analyze current published data on the link between cow's milk protein allergy and epileptic events, highlighting scientific evidence for any potential pathogenic mechanism and describing our clinical experience in pediatrics.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available [Expert review of clinical immunology](No link? Ask Salisbury Healthcare Library - please click here to request article).

### 5. Future of epilepsy treatment: Integration of devices

**Citation:** Future Neurology, October 2014, vol./is. 9/6(587-596), 1479-6708;1748-6971 (01 Oct 2014)

**Author(s):** Van Straten A.F., Jobst B.C.

**Language:** English  
**Abstract:** The use of devices in the treatment of epilepsy is an emerging therapy for those patients whose seizures are not controlled by medications. This article will discuss current treatment options with devices for vagus nerve stimulation, deep brain stimulation and responsive neurostimulation. Emerging therapies in noninvasive neurostimulation such as with trigeminal nerve stimulation, transcranial magnetic stimulation and transcranial direct current stimulation may prove to be promising solutions. Finally, new and enhanced techniques of drug delivery are discussed as well as other devices with potential use in the study and treatment of epilepsy.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available [ProQuest at Future Neurology](No link? Ask Salisbury Healthcare Library - please click here to request article).

### 6. Gender issues in antiepileptogenic treatments

**Citation:** Neurobiology of Disease, December 2014, vol./is. 72/PB(224-232), 0969-9961;1095-953X (December 01, 2014)

**Author(s):** Pitkanen A., Huusko N., Ndode-Ekane X.E., Kyyriainen J., Lipponen A., Lipsanen A., Sierra A., Bolkvadze T.

**Language:** English  
**Abstract:** Disease modification of epilepsy refers to the alleviation of epileptogenesis or comorbidities after genetic or acquired epileptogenic brain insults. There are currently 30 proof-of-concept experimental pharmacologic studies that have demonstrated some beneficial disease-modifying effects. None of these studies, however, has yet passed from the laboratory to the clinic. The International League Against Epilepsy and American Epilepsy Society working groups on antiepileptogenic (AEG) therapies recently released recommendations for conducting preclinical AEG studies, taking into account many of the critiques raised by previous study designs. One of the issues relates to the lack of analysis of AEG efficacy in both sexes. A review of the literature reveals that most of the preclinical studies have been performed using male rodents, whereas clinical study cohorts include both males and females. Therefore, it is important to determine whether sex differences should be taken into account to a greater extent than they have been historically at different phases of experimental studies. Here we address the following questions based on analysis of available experimental AEG studies: (a) whether sex differences should be considered when searching for novel AEG targets, (b) how sex differences can affect the preclinical AEG study designs and analysis of outcome measures, and (c) what factors should be considered when examining the effect of sex on outcome of clinical AEG trials or the clinical use of AEGs.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available [Neurobiology of disease](No link? Ask Salisbury Healthcare Library - please click here to request article).
7. Gene therapy for epilepsy

Citation: Epilepsy and Behavior, September 2014, vol./is. 38/(125-130), 1525-5050;1525-5069 (September 01, 2014)

Author(s): Simonato M.

Language: English

Abstract: Gene therapy may represent an effective alternative to standard pharmacological approaches for certain forms of epilepsy. Currently, the best candidates for this therapeutic approach appear to be epilepsies characterized by a focal lesion. Gene therapy has been attempted to produce antiepileptogenic (prevention of development of epilepsy in subject at risk after having received an epileptogenic insult), antiseizure (reduction of frequency and/or severity of seizures), and disease-modifying (alteration of the natural history of the disease) effects. An example of gene therapy aimed at producing antiepileptogenic effects is a combination therapy based on the supplementation of the neurotrophic factors brain-derived neurotrophic factor (BDNF) and fibroblast growth factor 2 (FGF-2). Antiseizure effects have been obtained by increasing the strength of inhibitory signals (by supplementing specific GABA<sub>A</sub> receptor subunits or inhibitory neuropeptides like galanin or neuropeptide Y) or by reducing the strength of excitatory signals (by knocking down NMDA receptor subunits). This review summarizes the results obtained to date using gene therapy in epilepsy models and discusses the challenges and the opportunities that this approach can offer for the treatment of human epilepsies.

Publication type: Journal: Review

Source: EMBASE

Full text: Available Epilepsy & behavior : E&B at No link? Ask Salisbury Healthcare Library - please click here to request article.

8. Genomic biomarkers of SUDEP in brain and heart

Citation: Epilepsy and Behavior, September 2014, vol./is. 38/(172-179), 1525-5050;1525-5069 (September 01, 2014)

Author(s): Glasscock E.

Language: English

Abstract: Sudden unexpected death in epilepsy (SUDEP) is the leading cause of epilepsy-related mortality, but how to predict which patients are at risk and how to prevent it remain uncertain. The underlying pathomechanisms of SUDEP are still largely unknown, but the general consensus is that seizures somehow disrupt normal cardiac or respiratory physiology leading to death. However, the proportion of SUDEP cases exhibiting cardiac or respiratory dysfunction as a critical factor in the terminal cascade of events remains unresolved. Although many general risk factors for SUDEP have been identified, the development of reliable patient-specific biomarkers for SUDEP is needed to provide more accurate risk prediction and personalized patient management strategies. Studies in animal models and patient groups have revealed at least nine different brain-heart genes that may contribute to a genetic susceptibility for SUDEP, making them potentially useful as genomic biomarkers. This review summarizes data on the relationship between these neurocardiac genes and SUDEP, discussing their brain-heart expression patterns and genotype-phenotype correlations in mouse models and people with epilepsy. These neurocardiac genes represent good first candidates for evaluation as genomic biomarkers of SUDEP in future studies. The development of validated reliable genomic biomarkers for SUDEP has the potential to transform the clinical treatment of epilepsy by pinpointing patients at risk of SUDEP and allowing optimized, genotype-guided therapeutic and prevention strategies.

Publication type: Journal: Review

Source: EMBASE

Full text: Available Epilepsy & behavior : E&B at No link? Ask Salisbury Healthcare Library - please click here to request article.

9. Is depression associated with an increased risk of treatment-resistant epilepsy? Research strategies to investigate this question

Citation: Epilepsy and Behavior, September 2014, vol./is. 38/(3-7), 1525-5050;1525-5069 (September 01, 2014)

Author(s): Kanner A.M.

Language: English

Abstract: Persons with epilepsy (PWE) have a higher risk of developing depressive disorders (DDs), and people
with primary DD have an increased risk of developing epilepsy. Furthermore, a lifetime history of DD has been associated with a worse response of the seizure disorder to pharmacotherapy and epilepsy surgery. The first part of this article reviews the literature of this problem with the intention of highlighting the neurobiologic pathogenic mechanisms operant in DD with a potential to facilitate the epileptogenic process and/or cortical hyperexcitability in humans and experimental animal studies of depression. They include the following: (i) a hyperactive hypothalamic-pituitary-adrenal axis and the associated structural and functional abnormalities of limbic structures, (ii) increased glutamatergic activity and decreased GABAergic and serotonergic activity, and (iii) immunologic disturbances. In the second part of this article, we suggest research strategies to test the hypothesis of whether depression worsens the course of epilepsy and identify the pathogenic mechanisms operant in this process. This article is part of a Special Issue entitled "NEWroscience 2013".

Publication type: Journal: Review
Source: EMBASE
Full text: Available Epilepsy & behavior : E&B at No link? Ask Salisbury Healthcare Library - please click here to request article.

10. Orientation and disorientation: Lessons from patients with epilepsy
Citation: Epilepsy and Behavior, December 2014, vol./is. 41/(149-157), 1525-5050;1525-5069 (December 01, 2014)
Author(s): Peer M., Lyon R., Arzy S.
Language: English
Abstract: Orientation in time, space, and person is a fundamental cognitive faculty and the bedrock of neurological and psychiatric mental status examination. Nevertheless, research in orientation and disorientation is neglected in both cognitive science and neuropsychiatry. Specifically, it is still unclear whether disorientations in time, space, and person represent a failure of the same system or merely share a common nomenclature and whether these three domains of orientation depend on different psychological and neural systems. Here, we analyzed descriptions of patients with specific orientation failures associated with circumscribed cortical lesions, with a primary focus on epilepsy. The form of disorientation is analyzed according to its specific domain, the underlying neuropsychiatric disorder, and its anatomical correlate. Disorientations in the different domains are classified as self-referenced (incorrect self-localization) or nonself-referenced (incorrect localization or knowledge of other places, events, and people). Analysis of the cognitive and neural systems disturbed in these patients suggests that disorientation in one or several domains may be related to a failure in a specific brain mechanism localized mostly in the right hemisphere, partially overlapping with the default mode network (mostly the medial and lateral parietal, medial temporal, and lateral prefrontal cortices), which processes essential self-related cognitive faculties such as orientation.
Publication type: Journal: Review
Source: EMBASE
Full text: Available Epilepsy & behavior : E&B at No link? Ask Salisbury Healthcare Library - please click here to request article.

11. Systems biology, complexity, and the impact on antiepileptic drug discovery
Citation: Epilepsy and Behavior, September 2014, vol./is. 38/(131-142), 1525-5050;1525-5069 (September 01, 2014)
Author(s): Margineanu D.G.
Language: English
Abstract: The number of available anticonvulsant drugs increased in the period spanning over more than a century, amounting to the current panoply of nearly two dozen so-called antiepileptic drugs (AEDs). However, none of them actually prevents/reduces the post-brain insult development of epilepsy in man, and in no less than a third of patients with epilepsy, the seizures are not drug-controlled. Plausibly, the enduring limitation of AEDs' efficacy derives from the insufficient understanding of epileptic pathology. This review pinpoints the unbalanced reductionism of the analytic approaches that overlook the intrinsic complexity of epilepsy and of the drug resistance in epilepsy as the core conceptual flaw hampering the discovery of truly antiepileptogenic drugs. A rising awareness of the complexity of epileptic pathology is, however, brought about by the emergence of nonreductionist systems biology (SB) that considers the networks of interactions underlying the normal organismic functions and of SB-based systems (network) pharmacology that aims to restore pathological networks. By now, the systems pharmacology approaches of AED discovery are fairly meager, but their
12. What are the similarities and differences between schizophrenia and schizophrenia-like psychosis of epilepsy? A neuropathological approach to the understanding of schizophrenia spectrum and epilepsy

Citation: Epilepsy and Behavior, September 2014, vol./is. 38/(143-147), 1525-5050;1525-5069 (September 01, 2014)
Author(s): Kandratavicius L., Hallak J.E., Leite J.P.
Language: English
Abstract: Temporal lobe epilepsy (TLE) and psychosis coexist more frequently than chance would predict. In this short review, clinical and neuropathological findings of schizophrenia, TLE, and psychosis of epilepsy are described to enhance our understanding of the noncoincidental association between these conditions. In addition, psychosis of epilepsy was included for the first time in the Diagnostic and Statistical Manual of Mental Disorders (DSM), in the recently launched 5th edition, and improvement in diagnostic criteria was highlighted. Since the hippocampus has long been considered an anatomical area involved in the pathophysiology of TLE and schizophrenia, neuropathological studies of psychoses of epilepsy may contribute to our understanding of the pathophysiology of psychosis in general. The discovery of shared mechanisms and/or affected neurochemicals in TLE and schizophrenia might disclose important clues on the vulnerability of patients with TLE to psychotic symptoms and be an opportunity for new treatment development.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Epilepsy & behavior : E&B at No link? Ask Salisbury Healthcare Library - please click here to request article.

Motor Neurone Disease Abstracts

13. Are there differences in the prevalence of palliative care-related problems in people living with advanced cancer and eight non-cancer conditions? a systematic review

Citation: Journal of Pain and Symptom Management, October 2014, vol./is. 48/4(660-677), 0885-3924;1873-6513 (01 Oct 2014)
Author(s): Moens K., Higginson I.J., Harding R.
Language: English
Abstract: Context. If access to effective palliative care is to extend beyond cancer patients, an understanding of the comparative prevalence of palliative care problems among cancer and non-cancer patients is necessary. Objectives. This systematic review aimed to describe and compare the prevalence of seventeen palliative care-related problems across the four palliative care domains among adults with advanced cancer, acquired immune deficiency syndrome, chronic heart failure, end-stage renal disease (ESRD), chronic obstructive pulmonary disease, multiple sclerosis, motor neuron disease, Parkinsons disease, and dementia. Methods. Three databases were searched using three groups of keywords. The results of the extraction of the prevalence figures were summarized. Results. The electronic searches yielded 4697 hits after the removal of 1784 duplicates. Of these hits, 143 met the review criteria. The greatest number of studies were found for advanced cancer (n = 57) and ESRD patients (n = 47), and 75 of the 143 studies used validated scales. Few data were available for people living with multiple sclerosis (n = 2) and motor neuron disease (n = 3). The problems with a prevalence of 50% or more found across most of the nine studied diagnostic groups were: pain, fatigue, anorexia, dyspnea, and worry. Conclusion. There are commonalities in the prevalence of problems across cancer and non-cancer patients, highlighting the need for palliative care to be provided irrespective of diagnosis. The methodological heterogeneity across the studies and the lack of non-cancer studies need to be addressed in future research.

Publication type: Journal: Review
Source: EMBASE
14. **Breathlessness in motor neurone disease: a review of the current strategies and gaps in the evidence.**

**Citation:** Current Opinion in Supportive & Palliative Care, September 2014, vol./is. 8/3(213-7), 1751-4258;1751-4266 (2014 Sep)

**Author(s):** Allcroft P

**Language:** English

**Abstract:** PURPOSE OF REVIEW: This review on breathlessness and motor neurone disease (MND) is important, as palliative care teams are increasingly becoming involved in the complex care of these patients at an earlier stage in their illness. Subtle cognitive and behavioural changes with MND may make management more challenging. Breathlessness is a distressing symptom, impacting on both patients and carers. Assessment and expectant management of breathlessness improves the quality of life (QoL) and may minimize hospital admission.

RECENT FINDINGS: Low-dose opioids improve the sensation of breathlessness, with minimal side-effects. It is well established that noninvasive ventilation (NIV) improves survival in patients with MND and also improves health-related QoL of patients with minimal or no bulbar symptoms. Preparation of advance care plans is essential to the provision of care in the final stages of illness in patients with MND and NIV use.

SUMMARY: Assessment of breathlessness and its successful management improves the QoL of patients with MND. Opioids in titrated doses may play a role in this. NIV improves survival in patients with respiratory failure with minimal or no bulbar symptoms and should be offered when appropriate. Preemptive education improves the uptake and understanding of the role of NIV.

**Publication type:** Journal Article

**Source:** MEDLINE

**Full text:** Available Current opinion in supportive and palliative care at No link? Ask Salisbury Healthcare Library - please click here to request article.

15. **Modeling motor neuron disease: The matter of time**

**Citation:** Trends in Neurosciences, November 2014, vol./is. 37/11(642-652), 0166-2236;1878-108X (01 Nov 2014)

**Author(s):** Arbab M., Baars S., Geijsen N.

**Language:** English

**Abstract:** Stem cell technologies have created new opportunities to generate unlimited numbers of human neurons in the lab and study neurodegenerative disorders such as amyotrophic lateral sclerosis (ALS) and spinal muscular atrophy (SMA). Although some disease hallmarks have been reported in patient-derived stem cell models, it is proving more difficult to recapitulate the full phenotypic extent of these disorders. The problem with these stem cell models lies in the disparity between the advanced age of onset of neurodegenerative disorders and the embryonic nature of the in vitro derived cell types. In this review we discuss experimental methods of in vitro aging of neural cell types as a means to elicit late-onset symptoms in induced pluripotent stem cell (iPSC) models of neurodegenerative disease.

**Publication type:** Journal: Review

**Source:** EMBASE

16. **Motor neuron disease and frontotemporal dementia: Sometimes related, sometimes not**

**Citation:** Experimental Neurology, December 2014, vol./is. 262/PB(75-83), 0014-4886;1090-2430 (December 01, 2014)

**Author(s):** Hardy J., Rogaeva E.

**Language:** English

**Abstract:** Over the last 5 years, several new genes have been described for both amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). While it has long been clear that there are many kindreds in which the two diseases co-occur, there are also many in which the diseases segregate alone. In this brief review, we suggest that keeping the loci which lead to both diseases separate from those which lead to just one gives a clearer conclusion about disease mechanisms than lumping them together. The hypothesis that this separation leads to is that loci which cause both ALS and FTD affect the autophagic machinery leading to damaged protein aggregation and those which lead to just ALS are mainly involved in RNA/DNA metabolism. Two of the genes causing FTD alone (CHMP2B and GRN) are associated with damaged autophagy/lysosomal pathway. However, the third FTD gene (MAPT) maps to a different pathway, which perhaps is not surprising, since it is associated with a different (not p62-related) brain pathology characterized by abnormal tau filaments. We conclude that the current state of knowledge points to common mechanisms responsible for susceptibilities specific to neuronal classes. This
includes the disruption of RNA metabolism in motor neurons and protein clearance, which is common between cortical and motor neurons.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available *Elsevier* at *Experimental Neurology*

### Multiple Sclerosis Abstracts

17. **Acquired channelopathies as contributors to development and progression of multiple sclerosis**  
**Citation:** Experimental Neurology, December 2014, vol./is. 262/PA(28-36), 0014-4886;1090-2430 (December 01, 2014)  
**Author(s):** Schattling B., Eggert B., Friese M.A.  
**Language:** English  
**Abstract:** Multiple sclerosis (MS), the most frequent inflammatory disease of the central nervous system (CNS), affects about two and a half million individuals worldwide and causes major burdens to the patients, which develop the disease usually at the age of 20 to 40. MS is likely referable to a breakdown of immune cell tolerance to CNS self-antigens resulting in focal immune cell infiltration, activation of microglia and astrocytes, demyelination and axonal and neuronal loss. Here we discuss how altered expression patterns and dysregulated functions of ion channels contribute on a molecular level to nearly all pathophysiologial steps of the disease. In particular the detrimental redistribution of ion channels along axons, as well as neuronal excitotoxicity with regard to imbalanced glutamate homeostasis during chronic CNS inflammation will be discussed in detail. Together, we describe which ion channels in the immune and nervous system commend as attractive future drugable targets in MS treatment.

18. **Adherence in multiple sclerosis (ADAMS): Classification, relevance, and research needs. A meeting report**  
**Citation:** Multiple Sclerosis, November 2014, vol./is. 20/13(1795-1798), 1352-4585;1477-0970 (20 Nov 2014)  
**Author(s):** Heesen C., Bruce J., Feys P., Sastre-Garriga J., Solari A., Eliasson L., Matthews V., Hausmann B., Ross A.P., Asano M., Imonen-Charalambous K., Kopke S., Clyne W., Bissell P.  
**Language:** English  
**Abstract:** Background: Adherence to medical interventions is a global problem. With an increasing amount of partially effective but expensive drug treatments adherence is increasingly relevant in multiple sclerosis (MS). Perceived lack of efficacy and side effects as well as neuropsychiatric factors such as forgetfulness, fatigue and depression are major determinants. However, research on adherence to behavioural interventions as part of rehabilitative interventions has only rarely been studied.Methods: In a one-day meeting health researchers as well as patient representatives and other stakeholders discussed adherence issues in MS and developed a general draft research agenda within a focus group session.Results: The focus group addressed four major areas: (1) focussing patients and their informal team; (2) studying health care professionals; (3) comparing practice across cultures; and (4) studying new adherence interventions.Conclusions: A focus on patient preferences as well as a non-judgemental discussion on adherence issues with patients should be at the core of adherence work.

19. **Cognitive impairment in multiple sclerosis**  
**Citation:** Brain and Nerve, October 2014, vol./is. 66/10(1201-1209), 1881-6096 (01 Oct 2014)  
**Author(s):** Ochi H.  
**Language:** Japanese  
**Abstract:** Cognitive impairment may occur in up to 70% of all patients with multiple sclerosis (MS). Although MS can affect various sites within the central nervous system, a specific pattern of cognitive deficits tends to be seen, especially in the early stages of the disease. These deficits include problems with attention, information processing speed, and working memory. This constellation of deficits can occur with any disease course, and a
minimal correlation has been found between physical disability assessed by EDSS and cognitive impairment. Many studies have shown that cognitive impairment is correlated with brain lesion volume, as well as brain atrophy. There are promising neuroimaging indicators that may be useful for identifying patients at risk for cognitive impairment, such as diffusion tensor imaging, the magnetization transfer ratio, and N-acetyl aspartate levels. Cognitive dysfunction is associated with adverse effects on quality of life, employment status, and social activities. Today, there are three avenues for treatment: disease modifying therapies, symptomatic treatments, and cognitive rehabilitation. Unfortunately, data linking therapeutic interventions are limited. A better understanding of cognitive function and its correlation with disease mechanisms will assist in providing a new comprehensive treatment strategy that begins immediately with the diagnosis of MS.

Publication type: Journal: Review
Source: EMBASE
Full text: Available Brain and nerve = Shinkei kenkyu no shinpo at No link? Ask Salisbury Healthcare Library - please click here to request article.

20. Current Developments in Pharmacogenomics of Multiple Sclerosis
Citation: Cellular and Molecular Neurobiology, October 2014, vol./is. 34/8(1081-1085), 0272-4340;1573-6830 (07 Oct 2014)
Author(s): Carlson R.J., Doucette J.R., Nazarali A.J.
Language: English
Abstract: Pharmacogenomics has a significant potential to impact how we treat diseases. It involves targeting genetically identifiable populations with therapeutic interventions that promises to yield immediate positive health outcomes with lower or no side effects. The 'trial and error' method of treatment will no longer be necessary with the successful implementation of personalized medicine. The following is an overview of some new developments in pharmacogenomics of multiple sclerosis, and how it has the potential to improve future treatment.
Publication type: Journal: Review
Source: EMBASE
Full text: Available Cellular and molecular neurobiology at No link? Ask Salisbury Healthcare Library - please click here to request article.

21. Current Role of Chemotherapy and Bone Marrow Transplantation in Multiple Sclerosis
Citation: Current Treatment Options in Neurology, November 2014, vol./is. 17/1(1-20), 1092-8480;1534-3138 (05 Nov 2014)
Author(s): Sola-Valls N., Sepulveda M., Blanco Y., Saiz A.
Language: English
Abstract: The range of available treatment options for patients with multiple sclerosis (MS) has expanded tremendously in recent years, adding further complexity to the therapeutic decision-making process. The first-generation therapies interferon beta and glatiramer acetate have been safely used for more than 20 years, but are only partially effective. Many of the newly approved MS therapies such as oral agents and monoclonal antibodies are selective immunosuppressants that appear to have improved efficacy and/or are more convenient, albeit in the absence of a long-term safety record. Although some are known to be associated with serious adverse effects, these treatments provide evidence-based therapeutic options for patients with suboptimal response or breakthrough disease. In this new scenario, non-selective immunosuppressive drugs and autologous hematopoietic stem cell transplantation are still present but likely play a more limited role than before. In this review, we briefly summarize the current, recent, and most imminent immunosuppressive therapies, and present an overall summary along with a discussion of their role in the current MS treatment scenario.
Publication type: Journal: Review
Source: EMBASE
Full text: Available Current Treatment Options in Neurology at No link? Ask Salisbury Healthcare Library - please click here to request article.

22. Daclizumab (anti-CD25) in multiple sclerosis
Citation: Experimental Neurology, December 2014, vol./is. 262/PA(44-51), 0014-4886;1090-2430 (December 01, 2014)
Author(s): Pfender N., Martin R.
Multiple sclerosis (MS) is a typical CD4 T cell-mediated autoimmune disease of the central nervous system (CNS) that leads to inflammation, demyelination, axonal damage, glial scarring and a broad range of neurological deficits. While disease-modifying drugs with a good safety profile and moderate efficacy have been available for 20 years now, a growing number of substances with superior therapeutic efficacy have recently been introduced or are in late stage clinical testing. Daclizumab, a humanized neutralizing monoclonal antibody against the alpha-chain of the Interleukin-2 receptor (IL-2Ralpha, CD25), which had originally been developed and approved to prevent rejection after allograft renal transplantation, belongs to the latter group. Clinical efficacy and safety of daclizumab in MS has so far been tested in several smaller phase II trials and recently two large phase II trials (combined 912 patients), and has shown efficacy regarding reduction of clinical disease activity as well as CNS inflammation. A phase III clinical trial is ongoing till March 2014 (DECIDE study, comparison with interferon (IFN) beta-1a in RRMS). Furthermore, the existing safety data from clinical experience in kidney transplantation and in MS appears favorable. Apart from the promising clinical data mechanistic studies along the trials have provided interesting novel insights not only about the mechanisms of daclizumab treatment, but in general about the biology of IL-2 and IL-2 receptor interactions in the human immune system. Besides blockade of recently activated CD25<sup>+</sup> T cells daclizumab appears to act through additional mechanisms including the expansion of immune regulatory CD56<sup>bright</sup> natural killer (NK) cells, the blockade of cross-presentation of IL-2 by dendritic cells (DC) to T cells, and the reduction of lymphoid tissue inducer cells.

**Publication type:** Journal: Review

**Source:** EMBASE

**Full text:** Available Elsevier at Experimental Neurology

### 23. Evidence for the efficacy of interferon beta-1b in delaying the onset of clinically definite multiple sclerosis in individuals with clinically isolated syndrome

**Citation:** Therapeutic Advances in Neurological Disorders, November 2014, vol./is. 7/6(279-288), 1756-2856;1756-2864 (12 Nov 2014)

**Author(s):** Freedman M.S.

**Language:** English

**Abstract:** The BEtaferon/BEtaseron in Newly Emerging MS For Initial Treatment (BENEFIT) trial assessed the efficacy of early versus delayed treatment with interferon beta-1b for patients with clinically isolated syndrome (CIS). Patients were randomly assigned to receive either interferon beta-1b 250 mug every other day (early treatment, n = 292) or placebo (delayed treatment, n = 176) for 2 years or until progression to clinically definite multiple sclerosis. Clinical and magnetic resonance imaging (MRI) outcomes were assessed after 2 years (at the end of the placebo-controlled phase) and then again at 3, 5, and 8 years post randomization. MRI assessments were made after 2, 3, and 5 years. The results showed a consistent advantage of early treatment across most clinical and MRI variables, although median Expanded Disability Status Scale scores remained consistently low, with no differences between groups. These findings suggest that early treatment with interferon beta-1b improves long-term outcomes for patients presenting with CIS.

**Publication type:** Journal: Review

**Source:** EMBASE

**Full text:** Available National Library of Medicine at Therapeutic Advances in Neurological Disorders

### 24. Glatiramer acetate to treat multiple sclerosis during pregnancy and lactation: A safety evaluation

**Citation:** Expert Opinion on Drug Safety, December 2014, vol./is. 13/12(1743-1748), 1474-0338;1744-764X (01 Dec 2014)

**Author(s):** Fragoso Y.D.

**Language:** English

**Abstract:** Introduction: Multiple sclerosis (MS) is a disease that mainly affects young adults who are of reproductive age. MS can lead to severe disability and is associated with worse prognosis in untreated patients. Although MS is not negatively affected by pregnancy itself, it may be a high-risk decision to leave a woman without treatment because she may get pregnant. Areas covered: This paper reviews the literature on pregnancies where the mother was exposed to glatiramer acetate. Few data are available on paternal exposure, but this does not seem to pose a problem due to the pharmacological characteristics of the drug. Only a limited amount of data from individual groups in the world is available in the literature. Expert opinion: TEVA Pharmaceuticals would need to open the database on pregnancy exposure to glatiramer acetate to allow for proper conclusions. Glatiramer
acetate is a drug of low risk in pregnancy (category B in the FDA classification) and may be a safe option for the treatment of women of fertile age with MS.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available **Expert opinion on drug safety** at No link? Ask Salisbury Healthcare Library - please click here to request article.

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25. **Laquinimod, an up-and-coming immunomodulatory agent for treatment of multiple sclerosis**  
**Citation:** Experimental Neurology, December 2014, vol./is. 262/PA(66-71), 0014-4886;1090-2430 (December 01, 2014)  
**Author(s):** Varrin-Doyer M., Zamvil S.S., Schulze-Topphoff U.  
**Language:** English  
**Abstract:** Laquinimod is a novel oral drug that is currently being evaluated for the treatment of relapsing-remitting multiple sclerosis (RRMS). Although the mode of action of laquinimod remains to be fully elucidated, current knowledge indicates that laquinimod exerts beneficial activities both on the peripheral immune system and within the central nervous system (CNS). The immunomodulatory properties have been deciphered primarily from studies of laquinimod in the animal model of multiple sclerosis, experimental autoimmune encephalomyelitis (EAE). Data indicate that laquinimod has a primary effect on innate immunity. Laquinimod modulates the function of various myeloid antigen presenting cell populations, which then downregulate proinflammatory T cell responses. Further, data also indicate that laquinimod acts directly on resident cells within the CNS to reduce demyelination and axonal damage. Results from clinical trials that tested laquinimod in RRMS demonstrated that it reduced relapse rate and the mean cumulative number of active lesions, and had a more marked reduction in disability progression than relapse rate. Laquinimod treatment was associated with an excellent safety and tolerability profile. These data indicate that laquinimod will offer a valuable new treatment option for RRMS patients.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available **Elsevier** at **Experimental Neurology**

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26. **Mode of action and clinical studies with alemtuzumab**  
**Citation:** Experimental Neurology, December 2014, vol./is. 262/PA(37-43), 0014-4886;1090-2430 (December 01, 2014)  
**Author(s):** Jones J.L., Coles A.J.  
**Language:** English  
**Abstract:** The lymphocyte depleting anti-CD52 monoclonal antibody alemtuzumab has been used in Cambridge, UK, as an experimental treatment of multiple sclerosis since 1991. One phase-2 trial (CAMMS-223) and two phase-3 studies (CARE-MS1 and CARE-MS2) have confirmed its efficacy in treatment-naive patients, and have established superiority over interferon beta-1a in patients who continue to relapse in spite of first-line therapy (Cohen et al., 2012; Coles et al., 2008; Coles et al., 2012a; Coles et al., 2012b). Despite causing a prolonged T cell lymphopenia, significant infections have not been an issue following treatment; rather alemtuzumab's primary safety concern is secondary autoimmunity, occurring up to five years after treatment and maximally at two years: 30% of patients develops thyroid autoimmunity, and 1% develops idiopathic thrombocytopenic purpura (ITP). In addition, 4 out of 1486 patients (< 0.3%) treated on the commercially sponsored studies developed glomerulonephritis. Two of these patients developed anti-glomerular basement membrane disease, a condition which may result in renal failure unless treated aggressively. In September 2013, the European Medicine Agency (EMA) ruled that the benefit-to-risk balance for alemtuzumab was favourable, approving it as a first-line therapy for adults with active relapsing remitting multiple sclerosis (under the trade name Lemtrada). Lemtrada is now also approved as a treatment of multiple sclerosis in Canada, Australia, Switzerland, Israel, Mexico and Brazil. However, in December 2013, Lemtrada failed to gain approval from the U.S. Food and Drug Administration (FDA), with concerns over trial design and safety stated as the main reasons. In this review we describe our local experience and explain the rationale behind its initial use as a treatment of multiple sclerosis and behind the design of the commercially sponsored trials, summarising their key findings. We also sum up our understanding of its mechanism of action.

**Publication type:** Journal: Review  
**Source:** EMBASE
27. Molecular mechanisms linking neuroinflammation and neurodegeneration in MS

Citation: Experimental Neurology, December 2014, vol./is. 262/PA(8-17), 0014-4886;1090-2430 (December 01, 2014)

Author(s): Ellwardt E., Zipp F.

Language: English

Abstract: Multiple sclerosis (MS) is an inflammatory demyelinating autoimmune disorder of the central nervous system (CNS) and one of the leading causes of neurological deficits and disability in young adults in western countries. Current medical treatment mainly influences disease progression via immunomodulatory or immunosuppressive actions. Indeed, MS research has been foremost focused on inflammation in the CNS, but more recent evidence suggests that chronic disability in MS is caused by neurodegeneration. Imaging studies show an early involvement of neurodegeneration as brain atrophy and gray matter lesions can be observed at disease onset. Thus, neuroprotective treatment strategies and the elucidation of the molecular mechanisms underlying neurodegeneration in MS have attracted the attention of the scientific community. Experimental autoimmune encephalomyelitis (EAE; the most commonly used animal model for MS), novel in-vivo imaging techniques such as two-photon microscopy and recently discovered molecular changes have offered new insights into the pathogenesis of neuroinflammation as well as neurodegeneration in MS. This review focuses on the interaction between components of the immune system and the neuronal compartment, as well as describing the most important molecular mechanisms that lead to axonal and neuronal degeneration in MS and EAE.

Publication type: Journal: Review

Source: EMBASE

Full text: Available Elsevier at Experimental Neurology

28. Multiple sclerosis and pregnancy prescriptions

Citation: Expert Opinion on Drug Safety, December 2014, vol./is. 13/12(1565-1568), 1474-0338;1744-764X (01 Dec 2014)

Author(s): Coyle P.K.

Language: English

Abstract: Multiple sclerosis (MS) is a major neurologic disorder which preferentially affects young women of childbearing age. In the last two decades, a number of disease-modifying therapies have become available to treat relapsing forms of MS. None of these agents is approved for use in pregnancy. The timing of treatment versus conception, and risk of drug pregnancy exposures, are frequent discussion topics when caring for MS patients. This editorial will try to put into context available data, approaches, controversies and future needs.

Publication type: Journal: Review

Source: EMBASE

Full text: Available Expert opinion on drug safety at No link? Ask Salisbury Healthcare Library - please click here to request article.

29. Plasticity of the motor system in multiple sclerosis

Citation: Neuroscience, December 2014, vol./is. 283/(222-230), 0306-4522;1873-7544 (December 06, 2014)

Author(s): Zeller D., Classen J.

Language: English

Abstract: Multiple sclerosis (MS) is a chronic neurological disease characterized by inflammation and degeneration within the CNS. Over the course of the disease, most MS patients successively accumulate inflammatory lesions, axonal damage, and a rather diffuse CNS pathology, along with an increasing degree of disability. Pharmacological treatment options which are currently approved for MS aim at limiting inflammation and decreasing the relapse rate, or at simply relieving symptoms. Established disease-modifying and immunosuppressive treatments are unable to prevent the accumulation of pathology in most patients over long-term. Therefore, therapies promoting the innate ability of the CNS to compensate for dysfunction resulting from brain injury might be highly beneficial in MS. As a precondition, however, development of such strategies requires well-grounded knowledge about the extent to which central plasticity is intact and accessible in MS patients, and whether it is functionally relevant at all. This review will focus on plasticity of the motor system in patients with MS. A number of functional imaging studies have assessed patterns of brain activation during simple motor tasks in MS patients and their relationship with CNS damage and motor function. Deeper insights about causal and
functional relationships were gained by neurophysiological techniques, predominantly by transcranial magnetic stimulation. In addition, and probably closest to rehabilitative approaches, practice-induced plasticity has been probed in a few studies. Altogether, there is growing evidence for a preservation of rapid-onset motor plasticity and for functionally relevant chronic reorganization processes, which might be limited by high CNS injury in advanced stages of the disease. Clinical implications of these findings with regard to the development and optimization of rehabilitative treatments in MS are discussed, as well as open questions which need to be addressed by future studies.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available Neuroscience at [No link? Ask Salisbury Healthcare Library - please click here to request article.](#)

**30. Remyelinating strategies in multiple sclerosis**  
**Citation:** Expert Review of Neurotherapeutics, November 2014, vol./is. 14/11(1315-1334), 1473-7175;1744-8360 (01 Nov 2014)  
**Author(s):** Luessi F., Kuhlmann T., Zipp F.  
**Language:** English  
**Abstract:** Multiple sclerosis (MS) is the most common chronic inflammatory demyelinating disorder of the CNS characterized by infiltration of immune cells and progressive damage to myelin sheaths and neurons. In recent years, the importance of the neuronal compartment in the early pathology of multiple sclerosis has become increasingly clear. Direct axonal damage within the early stages of inflammation as well as neuronal injury as a result of chronic demyelination are essential factors for the development of long-term disability in patients. Viewing MS as both inflammatory and neurodegenerative has significant implications for treatment, with remyelination of denuded axons to protect neurons from damage being necessary in addition to controlling inflammation. Here, we review recent molecular insights into key molecules and pathways controlling the differentiation of oligodendrocyte progenitor cells and the regenerative process of remyelination in MS and discuss the resulting options regarding remyelinating treatment strategies.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available Expert review of neurotherapeutics at [No link? Ask Salisbury Healthcare Library - please click here to request article.](#)

**31. Teriflunomide (Aubagio) for the treatment of multiple sclerosis**  
**Citation:** Experimental Neurology, December 2014, vol./is. 262/PA(57-65), 0014-4886;1090-2430 (December 01, 2014)  
**Author(s):** Bar-Or A.  
**Language:** English  
**Abstract:** Teriflunomide (Aubagio) is a once-daily oral immunomodulatory disease modifying therapy (DMT) presently approved in several regions, including Europe, North America, Latin America and Australia, for the treatment of relapsing forms of multiple sclerosis (RMS; RRMS). The therapeutic mode of action of teriflunomide in MS continues to be investigated. This review summarizes the main efficacy and safety results of the clinical trial program leading to teriflunomide's approval, highlights a number of practical clinical considerations, and overviews its presumed therapeutic mode of action (MOA) based on pharmacokinetic and pharmacodynamic observations and the growing body of teriflunomide-related in vitro, pre-clinical (animal model), and in vivo human studies.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available Elsevier at [Experimental Neurology](#)

**32. Treatment of Mood Disorders in Multiple Sclerosis**  
**Citation:** Current Treatment Options in Neurology, November 2014, vol./is. 17/1(1-11), 1092-8480;1534-3138 (05 Nov 2014)  
**Author(s):** Perez L.P., Gonzalez R.S., Lazaro E.B.  
**Language:** English  
**Abstract:** Multiple sclerosis (MS) is a chronic demyelinating disease of the central nervous system with a significant comorbidity with depressive disorders. Prevalence rates for major depressive disorder (MDD) range...
from 36% to 54% and the rate is around 22% for adjustment disorders. Selective serotonin reuptake inhibitors (SSRIs) are considered well-tolerated first-line treatment. Tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) are generally reserved for second-line use after SSRIs, because of sedating or anticholinergic side effects. SNRIs, with the exception of duloxetine, and combinations of newer antidepressants have failed to treat depression due to their side effects profile and frequent interaction with other drugs. Among SSRIs, sertraline is usually the first option, starting at 25 mg/day and increasing to 50 mg/day; and waiting a few weeks to assess drug effects before increasing the dose. The maximum is generally 200 mg/day in a single dose. Paroxetine is the second choice, starting at 10 mg/day for the first 5 days, and then at 20 mg/day thereafter. The maximum dose is about 50 mg/day in a single dose. Fluvoxamine is used at 100-200 mg/day, starting with 25 mg/day, and increasing 25 mg/day every 5 days until 200 mg/day is reached. We should take into account increasing blood level amounts of MS treatments (corticosteroids and cyclophosphamide) with fluvoxamine. With duloxetine, doses will be at 60-120 mg/day. The initial dose for depression is 40 mg/day in two doses; it can increase to 60 mg/day in one to two doses if necessary. The maximum dose is generally 120 mg/day. Duloxetine may increase liver problems through interaction with these MS treatments: teriflunomide, interferon beta-1a, and interferon beta-1b. Considering psychotherapy, only cognitive behavior therapy and mindfulness-based interventions have shown efficacy in improving depression disorders in MS. A comprehensive treatment for depression should include pharmacotherapy and psychotherapy.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available [Current Treatment Options in Neurology](https://linkinghub.elsevier.com/retrieve/pii/S1610669X14001320) at No link? Ask Salisbury Healthcare Library - please click here to request article.

### 33. Yoga for multiple sclerosis: A systematic review and meta-analysis

**Citation:** PLoS ONE, November 2014, vol./is. 9/11, 1932-6203 (12 Nov 2014)  
**Author(s):** Cramer H., Lauche R., Azizi H., Dobos G., Langhorst J.  
**Language:** English  
**Abstract:** While yoga seems to be effective in a number of neuropsychiatric disorders, the evidence of efficacy in multiple sclerosis remains unclear. The aim of this review was to systematically assess and meta-analyze the available data on efficacy and safety of yoga in patients with multiple sclerosis. Medline/PubMed, Scopus, the Cochrane Central Register of Controlled Trials, PsycINFO, CAM-Quest, CAMbase, and IndMED were searched through March 2014. Randomized controlled trials (RCTs) of yoga for patients with multiple sclerosis were included if they assessed health-related quality of life, fatigue, and/or mobility. Mood, cognitive function, and safety were defined as secondary outcome measures. Risk of bias was assessed using the Cochrane tool. Seven RCTs with a total of 670 patients were included. Evidence for short-term effects of yoga compared to usual care were found for fatigue (standardized mean difference [SMD] = 20.52; 95% confidence intervals (CI) = 21.02 to 20.02; p = 0.04; heterogeneity: I² = 60%; Chi² = 7.43; p = 0.06) and mood (SMD = 20.55; 95% CI = 20.96 to 20.13; p = 0.01; heterogeneity: I² = 0%; Chi² = 1.25; p = 0.53), but not for health-related quality of life, muscle function, or cognitive function. The effects on fatigue and mood were not robust against bias. No short-term or longer term effects of yoga compared to exercise were found. Yoga was not associated with serious adverse events. In conclusion, since no methodological sound evidence was found, no recommendation can be made regarding yoga as a routine intervention for patients with multiple sclerosis. Yoga might be considered a treatment option for patients who are not adherent to recommended exercise regimens.  
**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available ProQuest at PLoS ONE  
**Full text:** Available ProQuest at PLoS One

### Parkinson’s Disease Abstracts

#### 34. Bone health in Parkinson’s disease: a systematic review and meta-analysis

**Citation:** Journal of neurology, neurosurgery, and psychiatry, October 2014, vol./is. 85/10(1159-1166), 1468-330X (Oct 2014)  
**Author(s):** Torsney K.M., Noyce A.J., Doherty K.M., Bestwick J.P., Dobson R., Lees A.J.  
**Language:** English  
**Abstract:** Parkinson’s disease (PD) and osteoporosis are chronic diseases associated with increasing age. Single
studies have reported associations between them and the major consequence, namely, increased risk of fractures. The aim of this systematic review and meta-analysis was to evaluate the relationship of PD with osteoporosis, bone mineral density (BMD) and fracture risk. A literature search was undertaken on 4 September 2012 using multiple indexing databases and relevant search terms. Articles were screened for suitability and data extracted where studies met inclusion criteria and were of sufficient quality. Data were combined using standard meta-analysis methods. 23 studies were used in the final analysis. PD patients were at higher risk of osteoporosis (OR 2.61; 95% CI 1.69 to 4.03) compared with healthy controls. Male patients had a lower risk for osteoporosis and osteopenia than female patients (OR 0.45; 95% CI 0.29 to 0.68). PD patients had lower hip, lumbar spine and femoral neck BMD levels compared with healthy controls; mean difference, -0.08, 95% CI -0.13 to -0.02 for femoral neck; -0.09, 95% CI -0.15 to -0.03 for lumbar spine; and -0.05, 95% CI -0.07 to -0.03 for total hip. PD patients were also at increased risk of fractures (OR 2.28; 95% CI 1.83 to 2.83). This systematic review and meta-analysis demonstrate that PD patients are at higher risk for both osteoporosis and osteopenia compared with healthy controls, and that female patients are at greater risk than male patients. Patients with PD also have lower BMD and are at increased risk of fractures. 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 Highwire Press at Journal of neurology, neurosurgery, and psychiatry

35. Characterization of the thalamic-subthalamic circuit involved in the placebo response through single-neuron recording in Parkinson patients
Citation: Cortex, November 2014, vol./is. 60/(3-9), 0010-9452;1973-8102 (November 01, 2014)
Author(s): Frisaldi E., Carlino E., Lanotte M., Lopiano L., Benedetti F.
Language: English
Abstract: The placebo effect, or response, is a complex phenomenon whereby an inert treatment can induce a therapeutic benefit if the subject is made to believe that it is effective. One of the main mechanisms involved is represented by expectations of clinical improvement which, in turn, have been found to either reduce anxiety or activate reward mechanisms. Therefore, the study of the placebo effect allows us to understand how emotions may affect both behavior and therapeutic outcome. The high rate of placebo responders in clinical trials of Parkinson's disease provided the motivation to investigate the biological underpinnings of the placebo response in Parkinsonian patients. The placebo effect in Parkinson's disease is induced through the administration of an inert substance which the patient believes to improve motor performance. By using this approach, different behavioral and neuroimaging studies have documented objective improvements in motor performance and an increase of endogenous dopamine release in both the dorsal and ventral striatum. Recently, single-neuron recording from the subthalamic and thalamic regions during the implantation of electrodes for deep brain stimulation has been used to investigate the firing pattern of different neurons before and after placebo administration. The results show that the subthalamic nucleus, the substantia nigra pars reticulata, and the ventral anterior thalamus are all involved in the placebo response in Parkinson patients, thus making intraoperative recording an excellent model to characterize the neuronal circuit that is involved in the placebo response in Parkinson's disease as well as in other disorders of movement.
Publication type: Journal: Review
Source: EMBASE
Full text: Available Elsevier at Cortex

36. Drooling in Parkinson's disease: A review
Citation: Parkinsonism and Related Disorders, November 2014, vol./is. 20/11(1109-1118), 1353-8020;1873-5126 (01 Nov 2014)
Author(s): Srivanitchapoom P., Pandey S., Hallett M.
Language: English
Abstract: Parkinson's disease (PD) is a neurodegenerative disease causing both motor and non-motor symptoms. Drooling, an excessive pooling and spillover of saliva out of the oral cavity, is one of the non-motor symptoms in PD patients that produces various negative physical and psychosocial consequences for patients and their caregivers. At present, the pathophysiology of drooling in PD is not completely certain; however, impaired intraoral salivary clearance is likely the major contributor. There are neither standard diagnostic criteria nor standard
severity assessment tools for evaluating drooling in PD. In accordance with the possible pathophysiology, dopaminergic agents have been used to improve salivary clearance; however, these agents are not completely effective in controlling drooling. Various pharmacological and non-pharmacological treatment options have been studied. Local injection with botulinum toxin serotypes A and B into major salivary glands is most effective to reduce drooling. Future research to explore the exact pathophysiology and develop standard diagnostic criteria and standard severity assessment tools are needed to formulate specific treatment options and improve patient care.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available *Parkinsonism & related disorders* at No link? Ask Salisbury Healthcare Library - please click here to request article.

### 37. HDL and cognition in neurodegenerative disorders

**Citation:** Neurobiology of Disease, December 2014, vol./is. 72/PA(22-36), 0969-9961;1095-953X (December 01, 2014)  
**Author(s):** Hottman D.A., Chernick D., Cheng S., Wang Z., Li L.  
**Language:** English  
**Abstract:** High-density lipoproteins (HDLs) are a heterogeneous group of lipoproteins composed of various lipids and proteins. HDL is formed both in the systemic circulation and in the brain. In addition to being a crucial player in the reverse cholesterol transport pathway, HDL possesses a wide range of other functions including anti-oxidation, anti-inflammation, pro-endothelial function, anti-thrombosis, and modulation of immune function. It has been firmly established that high plasma levels of HDL protect against cardiovascular disease. Accumulating evidence indicates that the beneficial role of HDL extends to many other systems including the central nervous system. Cognition is a complex brain function that includes all aspects of perception, thought, and memory. Cognitive function often declines during aging and this decline manifests as cognitive impairment/dementia in age-related and progressive neurodegenerative disorders such as Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis. A growing concern is that no effective therapy is currently available to prevent or treat these devastating diseases. Emerging evidence suggests that HDL may play a pivotal role in preserving cognitive function under normal and pathological conditions. This review attempts to summarize recent genetic, clinical and experimental evidence for the impact of HDL on cognition in aging and in neurodegenerative disorders as well as the potential of HDL-enhancing approaches to improve cognitive function.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available *Neurobiology of disease* at No link? Ask Salisbury Healthcare Library - please click here to request article.

### 38. New treatments for the motor symptoms of Parkinson's disease

**Citation:** Expert Review of Clinical Pharmacology, November 2014, vol./is. 7/6(761-777), 1751-2433;1751-2441 (01 Nov 2014)  
**Author(s):** Vijverman A.-C., Fox S.H.  
**Language:** English  
**Abstract:** Levodopa remains the most potent drug to treat motor symptoms in Parkinson's disease (PD); however, motor fluctuations and levodopa-induced dyskinesia that occur with long-term use restrict some of its therapeutic value. Despite these limitations, the medical treatment of PD strives for continuous relief of symptoms using different strategies throughout the course of the illness: increasing the half-life of levodopa, using 'levodopa-sparing agents' and adding non-dopaminergic drugs. New options to 'improve' delivery of levodopa are under investigation, including long-acting levodopa, nasal inhalation and continuous subcutaneous or intrajejunal administration of levodopa. Long-acting dopamine agonists were recently developed and are undergoing further comparative studies to investigate potential superiority over the immediate-release formulations. Non-dopaminergic drugs acting on adenosine receptors, cholinergic, adrenergic, serotoninergic and glutamatergic pathways are newly developed and many are being evaluated in Phase II and Phase III trials. This article focuses on promising novel therapeutic approaches for the management of PD motor symptoms and motor complications. We will provide an update since 2011 on new formulations of current drugs, new drugs with promising results in Phase II and Phase III clinical trials, old drugs with new possibilities and some new potential strategies that are currently in Phase I and II of development (study start date may precede 2011 but are included
as study is still ongoing or full data have not yet been published). Negative Phase II and Phase III clinical trials published since 2011 will also be briefly mentioned.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available Expert Review of Clinical Pharmacology at No link? Ask Salisbury Healthcare Library - please click here to request article.

### 39. Novel pharmaceuticals in the treatment of psychosis in Parkinson's disease

**Citation:** Expert Review of Clinical Pharmacology, November 2014, vol./is. 7/6(779-786), 1751-2433;1751-2441 (01 Nov 2014)  
**Author(s):** Broadstock M., Ballard C., Corbett A.  
**Language:** English  
**Abstract:** Parkinson’s disease (PD) affects 10 million people worldwide. Half will develop psychosis, the majority experiencing hallucinations rather than delusions. Emergence of psychosis increases the likelihood of institutionalization and mortality. Where pharmacological treatment is warranted, options are limited. Most currently licensed atypical antipsychotics are ineffective or worsen motor symptoms in people with PD. This review provides an overview of the current landscape of treatments and the opportunities in emerging research. Clozapine is the only licensed antipsychotic with proven efficacy, although the associated side effects limit its use. With recent advances in understanding the role of serotonin, rational drug design approaches have delivered a novel pharmacological treatment with recently proven efficacy in clinical trials of people with PD and psychosis. Pimavanserin represents an important addition to treatment.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available Expert Review of Clinical Pharmacology at No link? Ask Salisbury Healthcare Library - please click here to request article.

### 40. Parkinson's disease in the limelight

**Citation:** Drugs of Today, September 2014, vol./is. 50/9(641-645), 1699-3993;1699-4019 (01 Sep 2014)  
**Author(s):** Graul A.I., Kamerkar S.  
**Language:** English  
**Abstract:** The 2014 Lasker-DeBakey Clinical Medical Research Award - one of three prestigious awards granted by the Lasker Foundation in recognition of scientists, clinicians and public servants who have made major advances in the understanding, diagnosis, treatment, cure or prevention of human disease - has been granted to two pioneers in the field of Parkinson's disease therapy. In spite of the availability of more than two dozen drugs and fixed-dose combination products to treat the symptoms of Parkinson’s disease - most notably the gold standard levodopa, a dopamine precursor - as well as nonpharmacological treatments like deep brain stimulation, many patients do not respond to available drugs or experience breakthrough symptoms, and the disease is ultimately incurable. This article reviews currently available therapies as well as biomarkers and novel diagnostics.

**Publication type:** Journal: Review  
**Source:** EMBASE  
**Full text:** Available Drugs of today (Barcelona, Spain : 1998) at No link? Ask Salisbury Healthcare Library - please click here to request article.

### 41. Safinamide for the treatment of Parkinson's disease

**Citation:** Expert Review of Clinical Pharmacology, November 2014, vol./is. 7/6(747-759), 1751-2433;1751-2441 (01 Nov 2014)  
**Author(s):** Kandadai R.M., Jabeen S.A., Kanikannan M.A., Borgohain R.  
**Language:** English  
**Abstract:** Parkinson’s disease (PD) is a neurodegenerative disease caused by a complex interaction of loss of dopaminergic and non-dopaminergic neurotransmitter systems. Drugs acting on the dopaminergic pathways are the mainstay of treatment for motor symptoms today. Safinamide (NW-1015) is a novel drug with multiple actions. It is a monoamine oxidase B inhibitor and improves dopaminergic transmission. In addition, it has antiglutamatergic effects and can thus reduce dyskinesias, which is a side effect limiting most dopaminergic therapy. In Phase III trials, safinamide has been found to be a useful adjunctive to dopamine agonists in early PD and has been shown to increase time without increasing troublesome dyskinesias when used as an adjunct to
levodopa in patients with advanced PD. A possible neuroprotective role in inhibiting PD disease progression is envisaged and warrants future studies.

Publication type: Journal: Review
Source: EMBASE

42. Sex differences in Parkinson’s disease and other movement disorders.
Citation: Experimental Neurology, September 2014, vol./is. 259/(44-56), 0014-4886;1090-2430 (2014 Sep)
Author(s): Smith KM, 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.
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Publication type: Journal Article, Review
Source: MEDLINE
Full text: Available Elsevier at Experimental Neurology

43. Stem cells and the treatment of Parkinson's disease
Citation: Experimental Neurology, October 2014, vol./is. 260/(3-11), 0014-4886;1090-2430 (October 01, 2014)
Author(s): Ali F., Stott S.R.W., Barker R.A.
Language: English
Abstract: Progress in Parkinson's disease (PD) research has been hampered by the lack of an appropriate model which exhibits the core pathology seen in the human brain. Recent advances in deriving cells with neuronal phenotypes from patients with neurodegenerative disorders through cellular reprogramming offer a unique tool for disease modelling and may help shed light on the molecular pathogenesis that drives the progression of the disease. This technology may also help in establishing platforms for drug screening and open up exciting new prospects for cell grafting. In this review, we will discuss progress made in differentiating stem cells into authentic dopamine neurons and where we stand with respect to clinical trials with these cells in patients with PD. We will also examine the various approaches used in cellular reprogramming and their differentiation into patient-specific midbrain dopamine neurons, with an emphasis particularly on modelling familial cases of PD to recapitulate disease phenotypes. This review will highlight some of the challenges that need to be addressed for this technology to have any potential clinical application in cell therapy and personalised medicine.
Publication type: Journal: Review
Source: EMBASE
Full text: Available Elsevier at Experimental Neurology

News

Stem cells could repair Parkinson’s damage
Friday 7th November 2014
"Stem cells can be used to heal the damage in the brain caused by Parkinson's disease," BBC News reports following the results of new Swedish research in rats.

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Information for Professionals

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How the MND Association can support you and your team  
Information and resources for health and social care professionals

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For MS Clinical Care and Research Professionals

**Parkinsons UK**  
Information for Professionals

**New Library Resources**

**Multiple Sclerosis – the facts**  
Sandra Amor and Hans van Noort  
Shelfmark: WL367  
Barcode: T026645

**The Clinical Practice of Neurological and Neurosurgical Nursing**  
Joanne V. Hickey  
ISBN: 978-1-4511-7267-6  
Shelfmark: WL650  
Barcode: T026713

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