**Meetings with FB re. prodrome and melatonin papers.**

**Meeting Notes.**

**06/05/2017**

**Prodrome paper**

PubMed library search @ [www.ncbi.nlm.nih.gov/pmc/](http://www.ncbi.nlm.nih.gov/pmc/)

Potential search terms (prodrome):

- epilepsy + pre-ictal

Possible prodromal symptoms to include in search terms:

MOOD DISORDERS

DEPRESSION

BEHAVIOURAL DISORDERS

IRRITABILITY

LIGHTHEADEDNESS

NAUSEA

VOMITING

PERSONALITY CHANGE

DYSPHORIC (MOOD)

Biochemical vs local electrical activity – how related?

**Primary generalized vs secondary generalized – any difference between prodromal symptoms?**

Consider section headings for prodrome paper. How to structure paper?

- Clinical - EEG - algorithm - other physiological (BOLD - MRI monitoring(?))

- Sub-divide technical

**Record search strategy(!)**

- Record limitations of search of Language etc. – (e.g.) English only

**Melatonin adverse effects paper**

Medication to induce sleep – investigate research on adverse affects of medical (oral) melatonin

Reviews of melatonin experiences specifically adverse effects

Potential effect on seizure, (?) - puberty onset??

Search terms:

- Adverse effects, side effects + melatonin

- Melatonin + epilepsy? increase in seizure rate?

- Melatonin + puberty?

- Melatonin + dizziness/headache/nausea?

- Exogenous melatonin/Oral melatonin

Synthetic melatonin agonists(?)

Agomelatine; Ramelteon; Tasimelteon; Circadin

**20/05/2017**

**Prodrome paper**

Does scope of any past research review coincide with the proposed review?

**How reliable are prodromal symptoms?**

~~Find out which closed loop systems are being manufactured and used – manufacturers (NeuroVista – Australian trial, 2013)~~

**Frequency and reliability of various prodromal systems(?)**

If symptoms are common symptoms in any case, how reliably can they be said to be genuine prodromes?

**Does duration of prodromal symptoms vary one from the other and what are their temporal relationships to seizure onset?**

~~Collect abstracts from most relevant papers send to FB to find full papers.~~

~~DuBois (2010) paper has concurrent EEG monitoring and patient seizure self-predicting. Abstract only - Ask FB for access.~~

**Melatonin paper**

For melatonin papers no specific time period of interest - include everything.

**27/05/2017**

**Points of action.**

~~Assemble abstracts for Melatonin papers (all) for FB and email.~~

Evaluate quality of papers - compare to preferred standard methodology (see example from FB paper)

~~Prodrome papers - list ones that you need full text and email FB.~~

**29/05/2017**

**Prodrome**

~~Percentages of specific symptoms i.e. number experiencing each symptom over total number of patients for each study.~~

**+ duration for each symptom where possible to extract.**

Stated as "where data available" in cases where data may be missing or incomplete.

**Controlled and uncontrolled data - comparing patients who experience prodromes and DO have a seizure and those that have prodromes but don't have a subsequent seizure (controlled) - some papers will show percentages some won't separate these figures out. What success rate do patients claiming prodromes have? What percentage of prodromes are and are not followed by seizures?**

**Which prodromes are the most successful at predicting seizure (if data available)?**

In some patients is it possible to have prodromes without seizure? Can these be said to be actual prodromes if no seizure then takes place? Possibly if seizure threshold is subsequently raised – see below.

Is it possible to have a  prodrome and NOT have a seizure. Something MAY happen to push seizure threshold over a certain level and so seizure doesn't take place. But this doesn't question the idea of prodrome itself?

But if seizures are NOT routinely followed by seizure it would question concept.

~~Combine papers with same symptoms and total percentage of patients over those studies who had prodrome.~~

**Compare symptoms that do and do not reliably predict seizures - have two tables, again with combined patient data over studies.**

Can set out in similar way to summary tables already compiled for prodromes.

**Are some symptoms reliable/statistically significant predictors (taking data from all studies together) and some not?**

EEG tables:

TODO:

~~Complete technological table comparing algorithms for sensitivity and specificity.~~

What studies should be done to link clinical symptoms to EEG side? - Is there sufficient clinical data to indicate correlation?

**Melatonin**

~~Record actual dose for melatonin both mg/kg and actual absolute (maximum dose) in new column where available.~~

~~Check library for paper for scales to determine quality of papers (Review subgroup)~~

~~Authors: Anand, Tong, Besag et al.~~

Criteria apply to randomized trials only and many might not be acceptable for purposes of this or another study on this basis.

Systematic reviews + proper criteria for conducting - FB will look up information for study. Educate yourself!!

**Next meeting Saturday 03/06 @ 3pm**

**03/06**

**Melatonin**

~~Separate random controlled trials from uncontrolled, separate tables and combined.~~

~~Percentage figures for melatonin table, and number n=x (where x is no patients)~~

Sam Cortese + Ian Wong + Paul Gringas

**Prodrome**

~~Split percentage table features that are reported 5% or more and second table for < 5%~~

~~Send list of recent reviews to FB (EEG side – probably 3)~~

~~Resend clinical prodrome list of papers required~~

Symptoms – keep separate for now – possibly group later (eg) dysphoric feeling anxiety, depression, behavioural change (restlessness, derealization etc).

~~Order in order of frequency by %.~~

**10/06/2017**

**Melatonin**

Placebo vs melatonin symptoms

Subtract placebo AE incidences from melatonin AE incidences for each AE and calculate percentage of total patients taking melatonin (NOT total number of patients in trial – ie exclude placebo group) from the result.

For controlled studies only.

What symptoms are of most concern for melatonin?

* Puberty
* Effect on seizures (though negative effect seems unlikely)
* Asthma

Long-term studies? Open studies – perhaps list for FB.

All controlled studies in one table and also a combined AE+ and AE- group.

Efficacy of melatonin as separate question.

Absence of long-term studies.

**Prodrome**

Seizure - Any clinical change accompanied by EEG change?

Continue with EEG feature time-to-seizure analysis if possible to extract information.

Epilepsy in search spelled incorrectly.

**17/06**

**Melatonin**

Separate melatonin adverse effects where there is and isn’t difference between melatonin and placebo into summary tables

Combined table and separate for each. For random controlled only.

Check for few additional papers added by FB today in melatonin group.

Continue with efficacy data

**Prodrome**

Email FB title of Petitmengin(?) paper on sensitivity training

Continue with time-to-seizure data for EEG

24/06/2017

Melatonin

Separate out table of adverse effects into table of studies with >=50 patients and a table for > 3months or longer studies.

Paper layout:

Introduction

Method

* Search strategy: search terms – database used – time period and inclusion and exclusion criteria (for example exclude animal studies) total no. papers retrieved, papers excluded and reason for exclusion, for example - adverse events mentioned but no specific data etc – relevant papers and reason for inclusion.
* Need to be VERY specific and clear
* Refer to table in other reviews for example (Anderson et al 2014 – A systematic review of peri-operative… Melatonin reviews sub category)
* Might exclude papers based on journal of publication – exclude low-quality ‘international’ for example
* Small number of patients or no new adverse effects in paper
* Include only sleep studies (cancer etc studies probably have little data in any case because short-term)

…

Prodrome

Split into two papers – clinical and EEG. One focused on clinical, one on EEG.

~~Clinical and EEG papers separate out for FB but maintain ratings. Investigate custom columns for identifying EEG or clinical~~.

If different but similar prodromes are listed, find papers where they are reported and check whether the separate prodromes are recorded separately – do the authors in any papers identify them separately. If not, is there an easy way to combine the symptoms into one group without compromising the data accuracy? How are authors distinguishing between similar symptoms or synonymous symptoms? Does it make sense to combine similar symptoms? Does it make sense to split groups ino more specific symptoms? Are there any frequently occurring symptoms currently included in the ‘other’ category that could be separated out?

New journal

Editorial assistant – spread sheet of papers [Title, Author. Date Submitted, Date resubmitted…etc]

Communicate with authors advising of required changes to submitted papers.