



MAUDSLEY LEARNING WEBINAR SERIES: The Psychiatry of Pandemics

Webinar 1: The Neuropsychiatric Legacy of Pandemic Influenza - Q&A

28th April 2020

Speaker panel:

- Dr Sotiris Posporelis
- Dr Thomas Pollak

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Question 1: Thank you for a fascinating discussion. Bearing in mind both the history and your own experiences during Covid, for future pandemics how could the field of neuropsychiatry be better prepared to respond? From a hospital setting through to a public health perspective.

Answer:

(Dr Thomas Pollak):

A few thoughts here:

- a) First and foremost – be better prepared to stop the spread of infection!
- b) I think there is probably a role for routine follow-up of severely affected individuals, particularly those who may be more at risk of developing psychiatric difficulties. At minimum I think this should probably include post-ITU patients.
- c) With all the concerns about post-infectious psychosis, plus the emerging realisation that a proportion (possibly fairly substantial) of SARS-COV2 infections may be asymptomatic, I think that there will be a role for antibody testing to index previous exposure in individuals presenting with new-onset psychiatric disorders. This may be mainly of interest on a research level initially, but it may be the most effective way to study the links between infection and neuropsychiatric outcomes.
- d) We are already planning to analyse blood samples from pregnant women who may have been infected – this will enable us in due course to look at associations with neurodevelopmental outcomes, if this turns out to be an area of concern.
- e) From what we've seen, there is probably less of a pronounced neuropsychiatric phenotype with COVID-19 than with most pandemic influenzas, so I think if the next pandemic is an influenza, we need to think about rapidly preparing mental health services for seeing these kinds of patients.



Question 2: Is there a difference in incidence of psychosis of children born during a pandemic vs those conceived during one and born after the peak is done?

Answer:

(Dr Thomas Pollak):

The most relevant evidence for this comes from studies looking at trimester effects. Early studies seemed to suggest greatest risk during the first trimester, although the risk still seems to be elevated for 2nd and 3rd trimester births. A systematic review of risk of prenatal maternal infection (looking at multiple infectious organisms) found a trend towards higher risk at the earlier stages of pregnancy (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3479084/>), but I don't think conception has been addressed specifically.

Question 3: Is there any historical evidence to suggest that an acute schizophrenia like syndrome associated with flu may then lead to a chronic encephalitis lethargica type picture, consistent with an inflammatory process in the brain and specifically in the Dopaminergic pathways?

Answer:

(Dr Thomas Pollak):

Not that I know of, but a really interesting idea! The largest series of acute psychoses of influenza is Menninger's 1926 series and in that, of the 50 acute 'dementia praecox' cases that were followed up for 5 years, none received an encephalitis lethargica diagnosis.

Question 4: I was just saying today that a lot of our post-COVID patients are not reporting fatigue. Which surprised us. But they are reporting problems with memory recall and language fluency. Anyone else seen this or has it been described in the literature?

Answer:

(Dr Thomas Pollak):

I haven't seen anything reported on this with regards to COVID, except an interesting thread on Twitter from someone experiencing similar symptoms! Funnily enough, I have seen quite a lot of people reporting severe fatigue, but also 'brain fog' symptoms. There is more on this with regards to influenza: infected mice certainly show cognitive problems, and there is an established literature on the effects of proinflammatory cytokines on these kinds of symptoms, so I think there's an argument that perhaps we should expect these – sometimes subtle, often transient – symptoms to affect some people in the current pandemic.

Question 5: How about those already with diagnosis of schizophrenia etc, if they are to be affected by the virus, what is their outcome?

Answer:

(Dr Thomas Pollak):

In the original series from the Spanish flu, infection could very clearly exacerbate pre-existing psychiatric diagnoses. We have seen or heard reported a number of cases of acute exacerbations of existing disorders which we think may have happened in association with COVID-19. There is good evidence that people with schizophrenia are



more vulnerable to infections: interestingly this has been shown not to have anything to do with one's genetic predisposition to schizophrenia (the so-called polygenic risk score) so may well have more to do with lifestyle issues or sociodemographic factors. More generally, people with schizophrenia have worse physical health outcomes, and sometimes the medications we prescribe can put them at risk of some adverse events which are relevant during a pandemic (e.g. clozapine and pneumonia).

Question 6: Do you think your research can shed any light on Post Lyme disease? If so, do you feel that some of the treatments being used for this problem could be used for Influenza, such as the ground-breaking work at Johns Hopkins with psychedelic drugs?

Answer:

(Dr Thomas Pollak):

I'm not aware of more than a handful of cases of psychosis as a manifestation of post-Lyme disease syndrome. My feeling is that the factors which shape post-infectious neuropsychiatric disorders are extremely varied and often include factors far beyond the biology of the infection. I think postviral fatigue is a fascinating phenomenon and that some of the factors are probably shared with the kind of fatigue that people get after Lyme disease too. I would be very cautious with psychedelics when it comes to treatment of psychosis, but it may well be that they will turn out to have a role in the treatment of other post-infectious neuropsychiatric presentations, including depression.

Question 7: Maternal Infection - isn't this related to the change on their microbiome and the research out of Germany into the long-term effects of maternal microbiome abnormalities and psychiatric illness?

Answer:

(Dr Thomas Pollak):

Increasingly the role of the microbiome in nearly every aspect of health is coming into focus – including for neurodevelopmental disorders and other psychiatric disorders. I'm not aware of any human studies addressing the issue with regards specifically to maternal influenza infection and psychosis risk, but there are definitely animal studies within the Maternal Immune Activation (MIA) paradigm that have looked at this issue: not only does MIA appear to have effects on the offspring microbiome, but microbiome-specific factors appear to determine the outcome of MIA in the offspring. There is a short summary of the few relevant studies in a section of this free-to-access review:

<https://www.frontiersin.org/articles/10.3389/fpsy.2019.00430/full>

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