

Neuropsychiatry of COVID-19 Infection in Adults and Children

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Historical Perspective

- Epidemic of encephalitis lethargica (EL) recognized around 1915
- New cases continue for 10-15 years
- Affected ~1.5 million individuals globally, with about 500,000 deaths
- Acute encephalitis was protean
- 80% of survivors developed parkinsonism within 10 years of recovery



Image Source: Wikipedia

(Cheyette & Cummings, 1995; Foley, 2018; Hoffman & Vilensky, 2017; Vilensky, 2011)

Historical Perspective

“The outcome for almost all EL patients was some form of tragedy: death, trouble with the law, inability to maintain stable relationships within their family or with others, physical disability, incarceration as children or young adults in mental hospitals and geriatric homes. The social aspects of EL concerned investigators and governments from around 1920, when it became clear that for a majority of patients – at least– there was no true post-EL period, as full recuperation could not be expected. ‘Recovery’ was often defined as the ability to work, even where this meant, for example, that a former teacher was now employed to undertake restricted gardening activities. Physical incapacity was a problem for most patients, whether because of parkinsonism or other neurologic symptoms, or because the long term mental effects – bradyphrenia, memory lapses, lack of concentration – prevented resumption of their pre-EL occupations.”

(Foley, 2018; Welfare Council of New York City, 1935)

Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: a systematic review and meta-analysis with comparison to the COVID-19 pandemic

Jonathan P Rogers*, Edward Chesney*, Dominic Oliver, Thomas A Pollak, Philip McGuire, Paolo Fusar-Poli, Michael S Zandi, Glyn Lewis, Anthony S David

- Cognition:
 - 27.9% with *acute* confusion → 18.9% with *post-illness* memory impairment
- Mood:
 - 32.6% with depressed mood *acutely* → 14.9% with *post-illness* depression
- Trauma:
 - 32.2% with PTSD at long-term follow-up
- Psychosis:
 - Acutely: 4.7% auditory hallucinations, 2% visual hallucinations, 3.9% persecutory beliefs
 - Long-term: 1% with auditory hallucinations, 2% persecutory beliefs
- Function:
 - 23.1% without return to work

(Rogers et al., 2020)

Blog | Journal of
Neurology, Neurosurgery & Psychiatry

The Neurology and Neuropsychiatry of COVID-19

Posted on [May 1, 2020](#) by [tnicholson](#)

Regularly updated repository of studies related to neuropsychiatric aspects of COVID-19,
maintained by the *Journal of Neurology, Neurosurgery & Psychiatry*

<https://blogs.bmj.com/jnnp/2020/05/01/the-neurology-and-neuropsychiatry-of-covid-19/>

COVID-19 → Neuropsychiatric Symptoms

- Prevalence of any neuropsychiatric manifestation in patients with COVID-19 = **22.5%**
- COVID-19 → incidence of any psychiatric disorder in first 3 months after infection is **18%** (with **6%** being new onset)

(Nalleballe et al., 2020; Taquet et al., 2020)



The TriNetX Global Health
Research Network

Image Source: trinetx.com

Neuropsychiatric Disorders → COVID-19

- Pre-existing neurologic disorder → COVID-19 death
- Pre-existing psychiatric disorder → COVID-19 infection after controlling for physical illness
- Pre-existing psychiatric disorder → increased risk of COVID-19 infection, hospitalization, and death

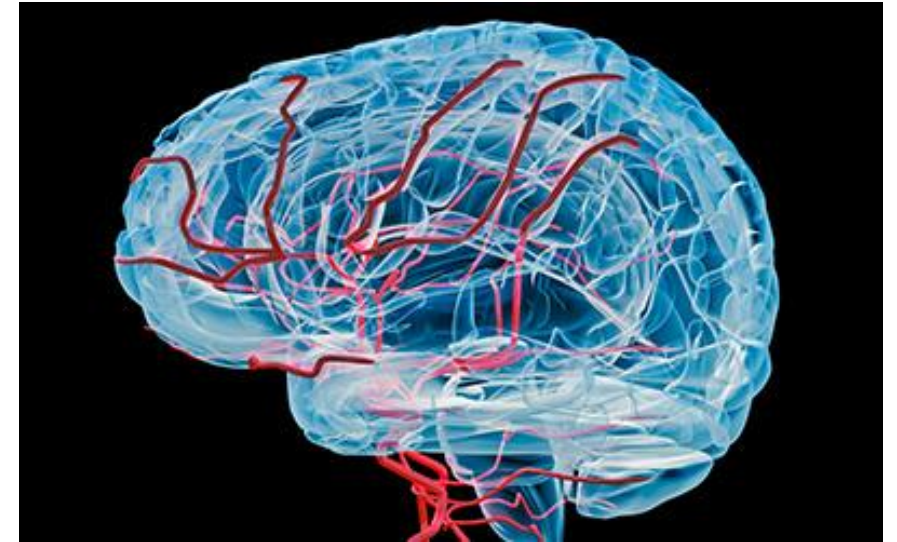


Image Source: alz.org

COVID-19 & Cognition

- 9-65% with delirium at initial presentation
- Delirium → risk of COVID-19 death
- 65-81% of survivors have post-hospitalization cognitive impairment
- Mild COVID-19 → cognitive decline
- Pre-existing dementia → COVID-19 infection and poor outcomes

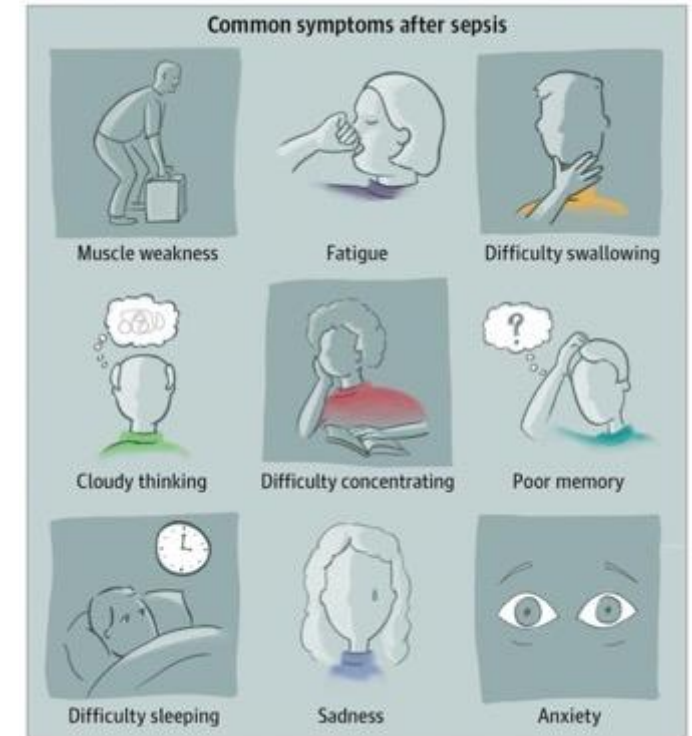


Image Source: JAMA on Twitter

COVID-19 & Depression

- 13.4 to 42% with depressed mood
- Associations: low health literacy, family member affected, perceived discrimination, mild infection, female sex, psychiatric history, hospitalized alone, recent NSAID use, age > 50, longer quarantine, milder infection
- Antidepressant exposure → decreased risk of intubation or death (HR 0.56)

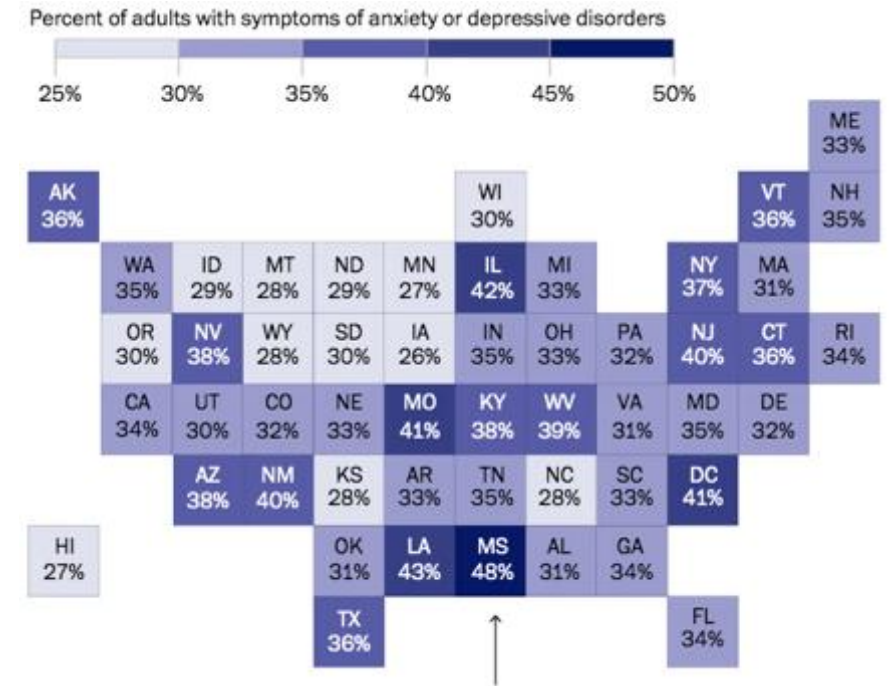


Image Source: Washington Post

(Alemanno et al., 2020; Dai et al., 2020; Hoertel et al., 2020; Jeong et al., 2020; Liguori et al., 2020; Liu et al., 2020; Mazza et al., 2020; Nguyen et al., 2020; Nie et al., 2020; Paz et al., 2020; Rogers et al., 2020; Sahan et al., 2020; Zhanga et al., 2020)

COVID-19 & Post-Traumatic Stress

- 6.5 to 96.2% trauma-related symptom prevalence
- But post-ICU PTSD prevalence is 19-22%
- PTSD symptom severity predicts duration of COVID-19 recovery
- Hospitalization, post-illness in-home medical care, female sex, psychiatric history, and delirium are associated with PTSD risk



Image Source: Healthline

COVID-19 & Psychosis

- ↑ schizophrenia incidence in Chinese clinic
- Case reports of anti-NMDA-R encephalitis
- Case series suggests some unique features (structured delusions 2+ weeks post-infection)
- Schizophrenia → increased COVID-19 mortality, but decreased ICU admission

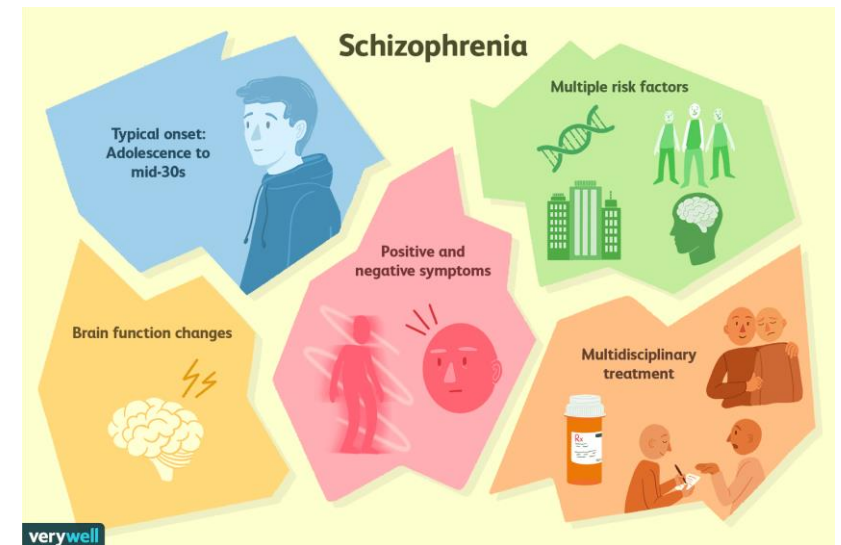
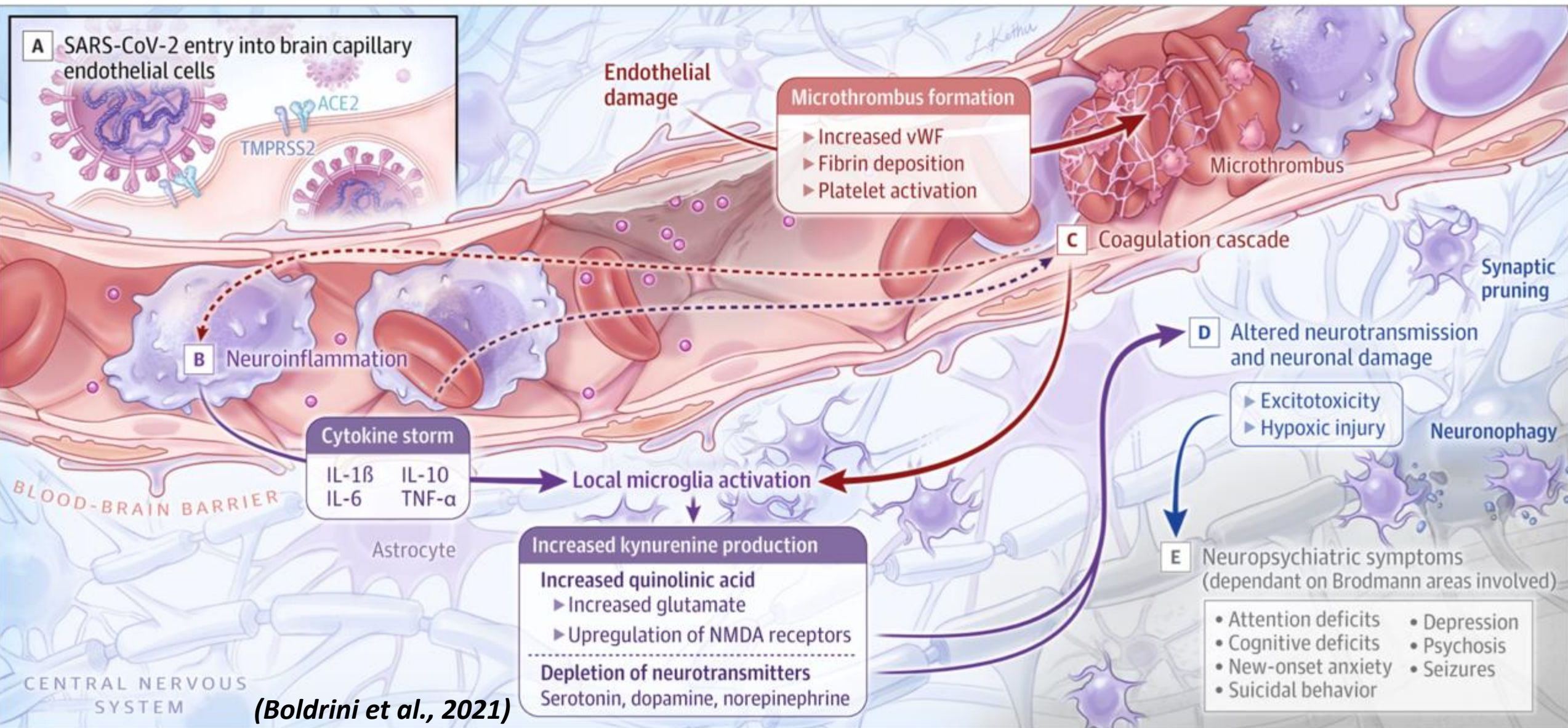


Image Source: Verywell Mind

(Bitan et al., 2021; Fond et al., 2020; Hu et al., 2020; Nemani et al., 2021; Panariello et al., 2020; Parra et al., 2020; Rogers et al., 2020)

Potential Pathogenic Mechanisms



Developmental Perspective

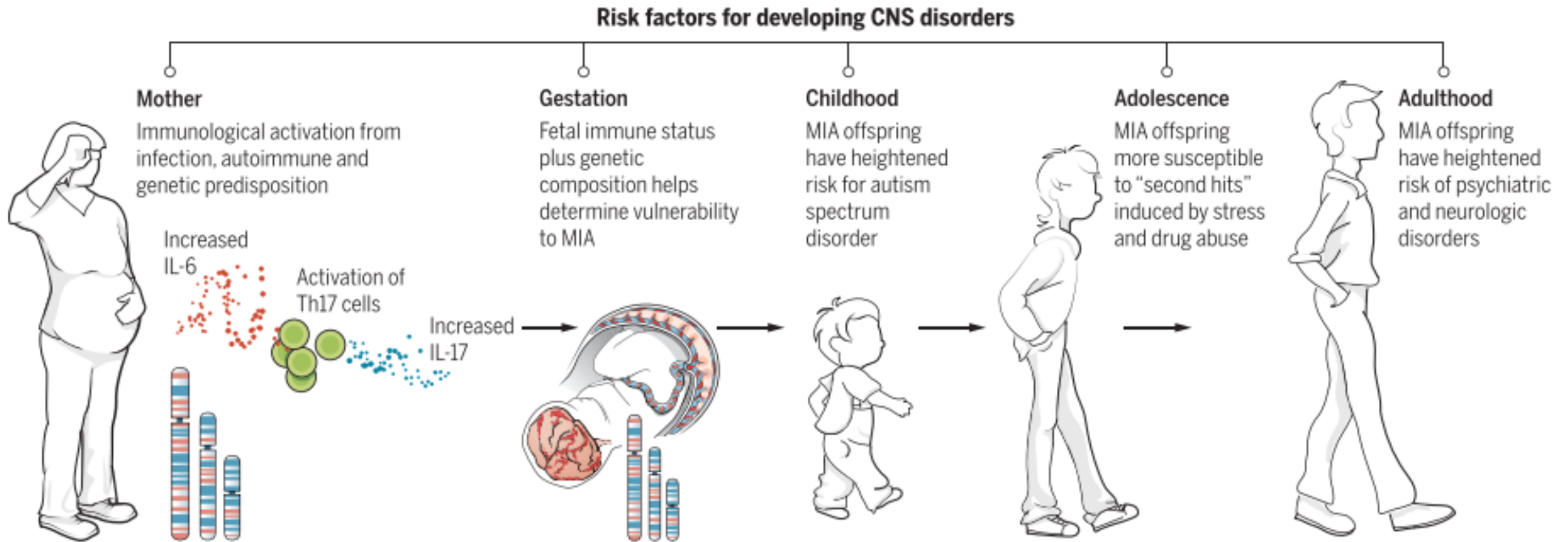


Fig. 1. MIA as a disease primer. This schematic depicts the current model for how MIA leads to psychiatric disorders in offspring. Infection leads to release of pro-inflammatory cytokines and activation of T_H17 cells in the mother's bloodstream (6, 19). A combination of genetic background, autoimmune status, and second hits during childhood and adolescence (including stress and drug abuse) combines with the consequences of maternal infection to increase the likelihood of offspring developing psychiatric disorders as adults (3, 6, 14, 37).

(Brown & Derkits, 2010; Estes & McAllister, 2016; Kępińska et al., 2020; Khandaker et al., 2012; Menninger, 1926)

Developmental Perspective

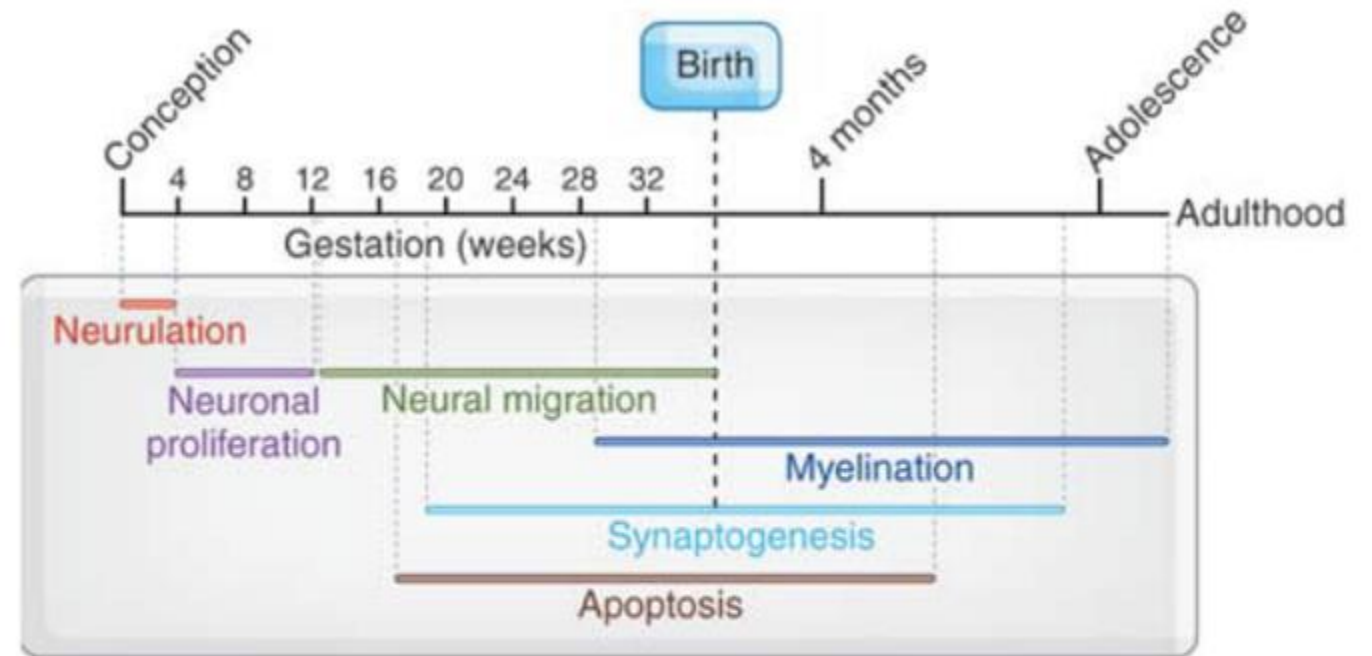
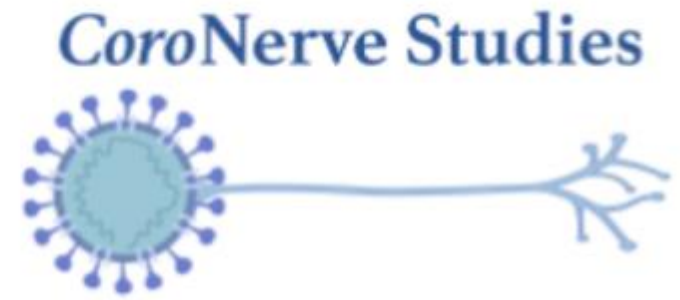
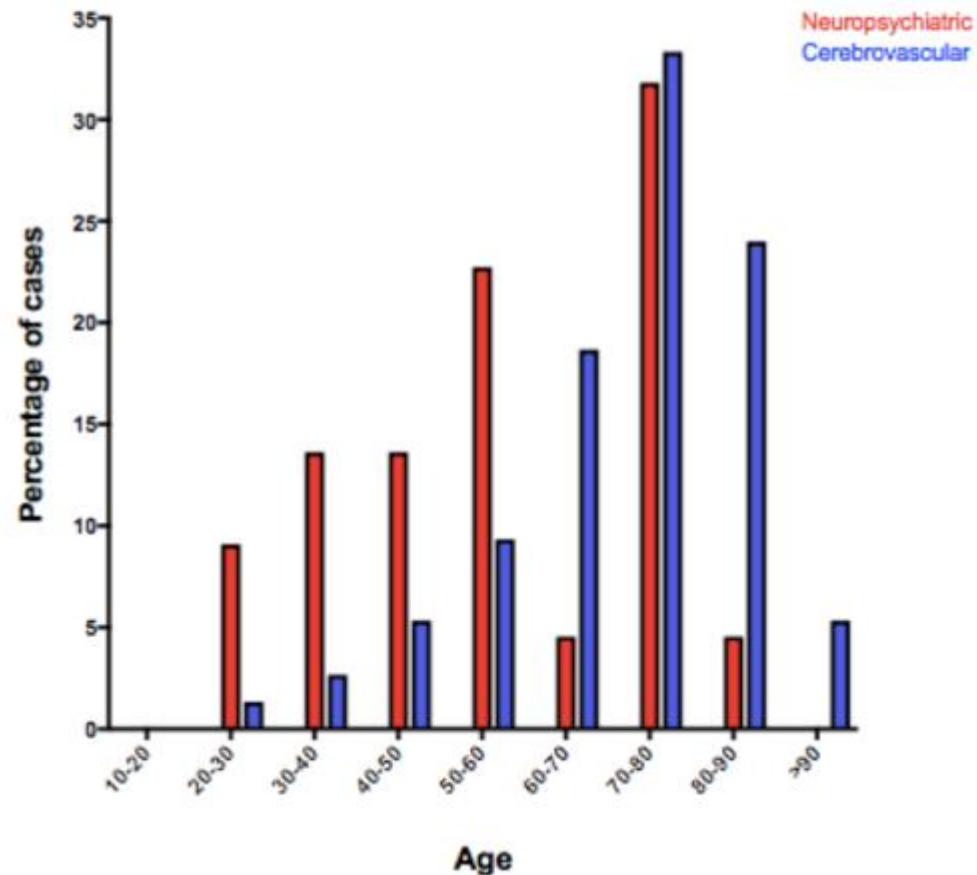


Figure 1. Timeline of major events in brain development. This diagram represents brain development beginning with neuroulation, and proceeding with neuronal migration, synaptogenesis, pruning, myelination, and cortical thinning. Reproduced with permission and modified from Giedd (1999) (Copyright 1999) American Psychiatric Association.

(Tau & Peterson, 2010)

Developmental/Lifespan Perspective



Altered mental status disproportionately observed in younger patients in UK-wide surveillance study

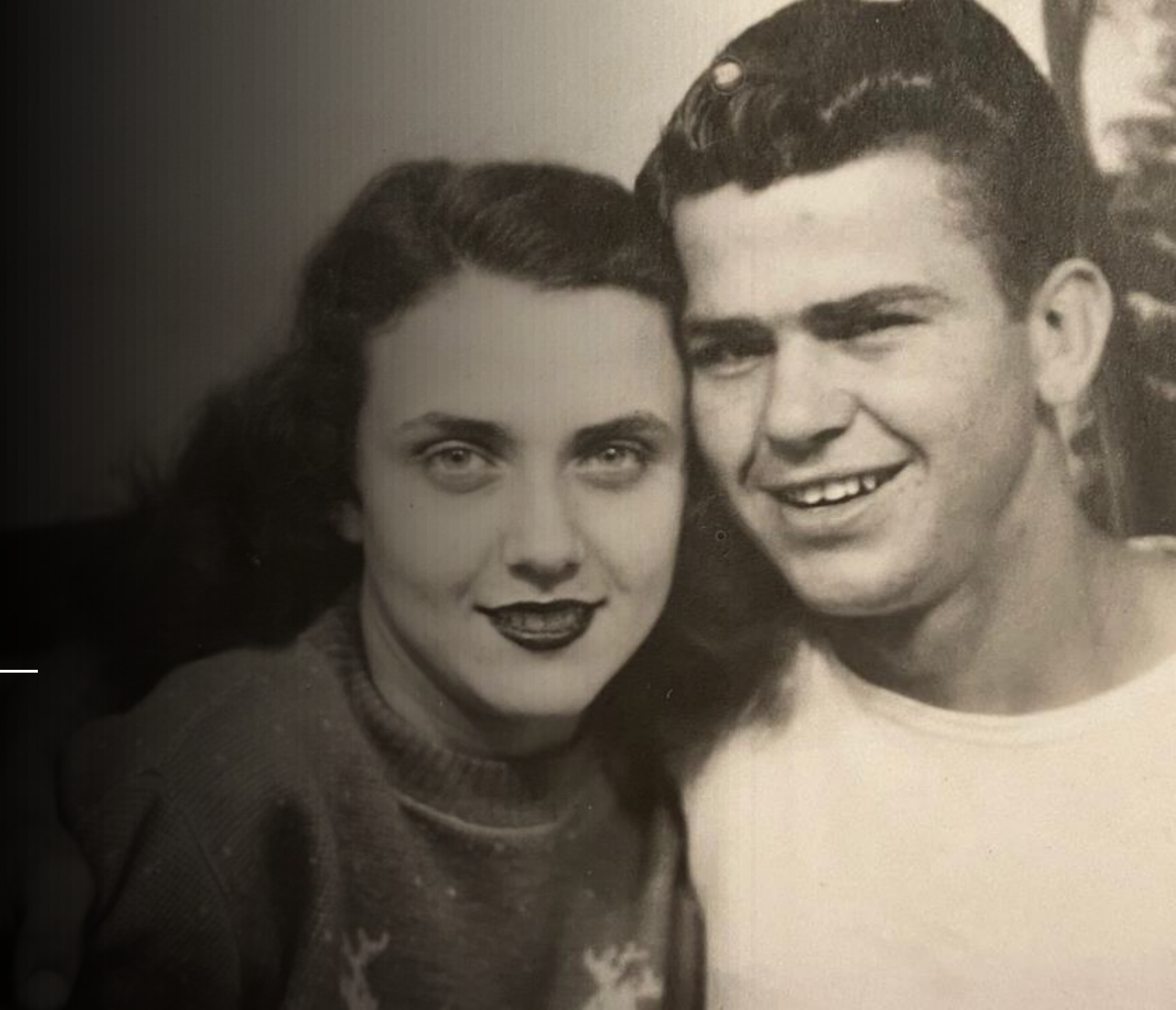
(Varatharaj, et al., 2020)

Summary

- COVID-19 is associated with risk for exacerbation or new-onset of several types of neuropsychiatric symptoms, particularly cognitive dysfunction, depression, and post-traumatic symptomatology
- Pre-existing neuropsychiatric disorders are associated with increased COVID-19 risk and worse prognosis, particularly vascular dementia and schizophrenia
- Long-term surveillance of COVID-19 survivors at various points in development will be needed to understand the full neuropsychiatric burden of the pandemic
- Pathogenic mechanisms are not fully understood, but mechanisms other than viral invasion of the CNS are likely at play
- Currently, there are no treatments specifically for COVID-19-related neuropsychiatric symptoms
- Going forward, we need to be prepared to screen and treat neuropsychiatric symptoms as usual, but likely on a much larger scale



In Memory of my Grandmother and all others
lost to COVID-19



Questions?

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