Trajectory of brain maturation and sex-specific cognitive abnormalities in early-onset psychosis

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Ruiz-Veguilla et al.,[1] in the January-March 2017 issue of *Revista Brasileira de Psiquiatria*, reported on ''sex-specific cognitive abnormalities in early-onset psychosis''. The study makes a contribution to our understanding of how schizophrenia might influence brain maturation and function. However, the authors based their conclusion on indirect evidence. The authors posited that the earlier peak of prefrontal cortex maturation seen in non-schizophrenia adolescent females will not be seen in female children and adolescents with first episode early onset psychosis (EOP). They also hypothesized that absence of the earlier peak of prefrontal cortex maturation in female children with EOP would result in no sex differences in working memory in the EOP population. Even though the authors confirmed their hypothesis in their sample, a number of important issues are worthy of discussion.

First, what is the exact nature of the sex-specific abnormalities in cognitive function that the authors concluded were present in their sample of patients with EOP? There were no sex differences in verbal working memory and auditory attention tests in the EOP sample and it appears that they based their conclusion on the finding that group effect (i.e. control vs. EOP) on verbal working memory and auditory attention was modified by sex. However, this interaction might just mean that sex has an effect on cognition in controls but not patients. Furthermore, at the end of the first paragraph in the discussion section, the authors wrote that ''less impairment in verbal working memory and auditory attention was present only in girls with EOP'' but this statement is not supported by Table 4 of the paper. An important question that should also be asked is: does schizophrenia slow brain maturation at the same rate in female and male adolescent patients? As acknowledged by the authors, their study cannot answer this question due to its cross-sectional design.

In terms of future direction, it would be desirable for Ruiz-Veguilla et al. to follow this cohort of patients and controls longitudinally (and if possible increase the sample size). Longitudinal follow-up with serial assessments of cognitive function as well as imaging modalities will be helpful to elucidate the nature of any sex-specific cognitive abnormality in early-onset psychosis and underlying mechanisms by which schizophrenia affects brain maturation. It may also be beneficial to assess cognition with the MATRICS Consensus Cognitive Battery, which was designed to ensure that cognitive testing is consistent and comparable across studies.[2]

Disclosure

The author reports no conflicts of interest.

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Zika virus infection followed by a first episode of psychosis: another flavivirus leading to pure psychiatric symptomatology

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Zika virus (ZIKV), a flavivirus primarily transmitted by *Aedes* mosquitoes, represents a major public health concern. ZIKV infection, previously considered a self-limited febrile exanthematic disease, leads to serious neurologic complications.[1]

Microcephaly and extensive brain damage can result from congenital ZIKV infection. An association with Guillain-Barre Syndrome was suggested after the French Polynesia outbreak,[2] and reports from endemic areas suggest that acute ZIKV infection leads to numerous central nervous system (CNS) complications. Considering the complexity of CNS function, we can expect a variety of clinical manifestations, even purely psychiatric symptoms.

A 17-year-old boy was transferred to our psychiatric emergency ward for evaluation of a first-episode psychosis (FEP). He had no significant health history or previous psychiatric history. Ten days prior to admission, he suddenly presented paranoid delusions and vivid auditory, somatic and olfactory hallucinations. He showed intense anxiety and panic-like symptoms, alternating with moments of inadequate behavioral disinhibition. Symptoms also included sleeplessness, increased speech production, vocal mannerisms and refusal to eat. A distinct period of altered mood was negated. Upon admission he was fully conscious with no attention deficits, disoriented

about the time and place, afraid, suspicious and speaking incoherently. Physical and neurological exams were otherwise normal. Initial workup included hematological, toxicological, neuroradiologic and electroencephalographic assessments, which were all within normal range. A febrile rash – followed by pruritus, myalgia, arthralgia, periocular pain and posterior cervical adenopathy, which began 14 days before the onset of the behavioral symptoms and remitted after a week – was then reported by his parents.

We extended the investigation to rule out other medical conditions leading to the psychotic episode. All CSF parameters were within the normal range. In peripheral blood we detected positive dengue virus (DENV) in ELISA, IgM, and IgG tests; the NS1 antigen was undetectable and RT-PCR was negative for DENV. RT-PCRs for ZIKV resulted positive in multiple blood samples. An intense cross-reaction was observed across DENV and ZIKV ELISA titers,[3,4] leading us to conclude that this was the case. After five days of Haloperidol with no response, the prescription was changed to Risperidone 2 mg/day and remission was achieved in three days. The patient was discharged and medication was tapered off after 3 weeks. No relapse in symptoms was noted during one year of follow-up in our specialized FEP outpatient service.

To the best of our knowledge, this is the first report in which psychiatric symptoms were the only complication of acute ZIKV infection. There is much evidence of psychiatric symptomatology in viral infections. Dengue-related manic and psychotic episodes have been described in which symptoms suggesting encephalitis or encephalopathy were not seen – thus supporting flavivirus' role in inducing purely behavioral symptoms. Cases in which DENV infections have led to neuropsychiatric complications are numerous, well established in the literature and more commonly diagnosed than in regular clinical practice.[5]

Neuroimmune mechanisms leading to psychosis during acute CNS stress is an open and prolific field for research. On the clinical front, mental health professionals dealing with emergency psychiatry and FEP must have a high grade of suspicion to avoid underrecognizing particular – and self-limited – conditions.

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The authors report no conflicts of interest.

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Lack of protocols for handling missing sessions of transcranial direct current stimulation (tDCS) in depression trials: what are the risks of neglecting missing sessions?

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Transcranial direct current stimulation (tDCS) represents a potential effective treatment for depression and has already shown encouraging results.[1,2] Given that tDCS requires the subject's presence, the probability of missed sessions is high, especially in depressed subjects. However, there is no consensus about the effects of missed sessions on tDCS efficacy.

A recent study reported that 60% of depressive subjects in a tDCS study missed at least one visit out of ten.[3] It is also known that the intensity and, probably, the frequency of tDCS sessions significantly increase the effectiveness of tDCS.[3] Missing sessions are very frequent, and how to deal with them is an issue of high relevance. Unfortunately, there is a glaring lack of information about missed sessions in tDCS trials for depression, even though this can lead to possible changes in the results and their interpretation. Thus, we can infer that missing sessions is potentially harmful to a complete response by the depressed individual.

We performed a systematic review of the PubMed/MEDLINE database between 2005 and 2015 regarding methods used to handle missing sessions in trials. Of the eight included trials, only three provided some information about missing sessions (Table 1). The two first trials[4,5] mentioned the maximum number of sessions that could be missed (no more than two non-consecutive sessions) before excluding the subject and how they handled such cases. Zanão et al. stated that missing two sessions in the acute treatment phase might not change the final result,