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.

Gabriel Elias Corrêa-Oliveira,[1] Julia Lopes do Amaral,[1] Benedito Antônio Lopes da Fonseca,[2] Cristina Marta Del-Ben[1]

[1]*Serviço de Emergências Psiquiátricas, Departamento de Neurociências e Ciências do Comportamento, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, Brazil.* [2]*Divisão de Moléstias Infecciosas e Tropicais, Departamento de Clínica Médica, Faculdade de Medicina de Ribeirão Preto, Universidade de São Paulo, Ribeirão Preto, SP, Brazil*

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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,

Table 1 RCTs characteristics using tDCS for depression

Study	Subjects (n)	Current (mA)	Duration (min)	No. sessions	Anode/ Cathode	Dropout	Missing sessions	Positive outcome
Fregni 2006[6]	10	1	20	5	F3/RSO	0	NM	Yes
Boggio 2008[7]	40	2	20	10	F3/RSO	0	NM	Yes
Loo 2010[8]	40	1	20	5(10*)	F3/RSO	6	NM	Yes
Brunoni 2013[4]	120	2	30	12	F3/F4	17	Yes† (>2 sessions)	Yes
Brunoni 2014[5]	37	2	30	10	F3/F4	21	Yes† (>2 sessions)	No
Ho 2014[9]	14	2	20	10	F3/F8 or F8/F3	2	NM	Yes
Segrave 2014	27	2	24	5	F3/F8	1	Yes*	Yes
Bennabi 2015[10]	24	2	30	10	F3/RSO	1	NM	No

NM= not mentioned; RSO = right supraorbital area; RCT = randomized controlled trial; tDCS = transcranial direct current stimulation.
* Previous session result was reported when a patient missed one session.
† Participants were allowed to miss two nonconsecutive visits; in such cases, extra tDCS sessions were performed to complete the total number of sessions.

although they point out the need for more studies exploring the impact of a higher number of absences on the treatment of depression disorders. The management of this methodological issue is fundamental for scientific development.

Another question is whether there is a relation between the efficacy and timing of a missing session. Do subjects who missed sessions other than at the beginning of the trial have the same results? What about the lasting effects, are they affected by the timing of missing sessions as well? One study made up for the missed tDCS sessions at the end of the protocol.[4] This evidently shows concern with the methodological approach but, again, leads us to question whether the results can be interpreted in the same way for these subjects.

Segrave et al.[11] considered the last observation carried forward as a way of dealing with the missing data due to missed sessions. This is a conservative method that can minimize the good results of tDCS. Moreover, details about how many subjects missed one or more sessions were not provided. The majority of the available articles made no mention of methodological concerns over this issue.

Considering that depressed individuals have difficulty in performing their daily activities, not only having a well-designed plan to address missing sessions but also building an adaptive protocol requires urgent attention. Therefore, clear definitions about how to address them and well-designed guidelines are needed. A new trial specifically designed to assess tDCS efficacy according to the number of missing sessions would certainly help establish a comprehensive framework for informing how many sessions can be missed without having a major impact on the subject.

Rivadávio F. Amorim,[1] Monique Gomes da Silva Scalco,[1,2] Maria Cecília de Freitas-Ferrari,[1,2] Tiago Freitas,[1] Heitor Moreno,[3] Aline Patrícia Brietzke,[4] Joaquim Brasil-Neto[5]

[1]*Programa de Pós-Graduação em Ciências Médicas, Faculdade de Medicina, Universidade de Brasília (UnB), Brasília, DF, Brazil.* [2]*Laboratório de Psiquiatria, Faculdade de Medicina, UnB, Brasília, DF, Brazil.* [3]*Laboratório de Farmacologia Cardiovascular, Universidade Estadual de Campinas (UNICAMP), Campinas, SP, Brazil.* [4]*Laboratório de Dor e Neuromodulação, Departamento de Pesquisa Clínica, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul (UFRGS), Porto Alegre, RS, Brazil.* [5]*Laboratório de Neurociências e Comportamento, Departamento de Ciências Fisiológicas, UnB, Brasília, DF, Brazil*

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