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Invited commentary

Leveraging neurological "soft" signs in the prediction of schizophrenia: A 35-year follow-up case illustration

Urvakhsh Meherwan Mehta [a,*], Matcheri S. Keshavan [b]

[a] Department of Psychiatry, National Institute of Mental Health & Neurosciences (NIMHANS), Bangalore, India
[b] Department of Psychiatry, Beth Israel Deaconess Medical Center and Massachusetts Mental Health Center, Harvard Medical School, Boston, MA, USA

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1. Introduction

In clinical practice, we often encounter patients who do not precisely meet criteria for any given disorder, resulting in the implementation of the "catch-all" categories of "not otherwise specified" diagnoses. The most important challenge in making such diagnoses is the limited data to support longitudinal course and treatment outcome predictions (Redish and Gordon, 2016). In this context, it is not uncommon to encounter patients who present with a multitude of catatonic symptoms, that remit with treatment, leaving behind no clinical signs or symptoms to permit a confident diagnosis of specific affective, non-affective or organic psychoses. The ensuing clinical challenge is in deciding the appropriate long-term pharmacotherapy strategy.

Recent incremental advances in the field of data-driven predictive and computational psychiatry promise more accurate diagnostics, treatment selection and prediction of treatment response (Huys et al., 2016). One of the critical components of good prediction models is the use of relevant data. In the era of digital phenotyping (Hsin et al., 2018) and ecological momentary assessments (Myin-Germeys et al., 2018), it is vital not to discount the age-old practice of a thorough physical exam. While careful physical examination provides crucial clues to organic etiology of psychiatric disorders (Patten, 1988), it also provides a window to their neurodevelopmental origins and enables identification of possible prognostic markers through the detection of 'soft' neurological signs (Bombin, 2005).

Primitive or infantile reflexes are one such category of 'soft' signs, which are easily elicited and can provide important diagnostic and prognostic information (Sanders and Keshavan, 1998). They represent protective motor responses that are normal during early development, inhibited later in childhood and resurface with cerebral (frontal) dysfunction (Schott, 2003) that is characterized by poor cortical inhibitory tone (Mehta et al., 2019). In this report, we emphasize the utility – established over a period of 35 years – of primitive reflexes (palmomental and glabellar tap) in predicting the diagnosis and selecting treatment in a patient with catatonia.

2. Case report

Mrs. M, a 28-year-old married lady presented to the emergency services (in 1984) with three months history of abnormal behaviors characterized initially (first two weeks) by restlessness, intermittent over-talkativeness and tearfulness, and bizarre gesturing. In the next two and a half months, she was seen to be withdrawn, maintaining postures for long, and refused food. On examination in the emergency ward, she was immobile and mute, her eyes were open, facial grimacing was present along with psychological pillow – stereotyped posturing of shoulder and neck muscles, as she remained supine in bed with her head few inches off the pillow (Mehta et al., 2011), and waxy flexibility – a feeling of plastic resistance as the examiner moved the patient's body (Casey and Kelly, 2011). Physical examination revealed no systemic abnormalities. However, she was observed to have bilateral palmomental reflexes (a reflex activity of the mentalis muscle with a noxious stimulus applied by a key scratch on the palm), increased blink rate and a positive glabellar tap – a failure of habituation of blinking with successive taps on the glabella (see Fig. 1). Her hemogram was unremarkable, and the serologic test for syphilis was negative. Her catatonic symptoms dramatically remitted after she received just one treatment session of bitemporal electroconvulsive therapy. Subsequently, her mental status examination revealed no delusions, hallucinations, mood symptoms or other behavioral abnormalities. While the diagnosis of catatonia was undisputed, there was limited clinical evidence to ascribe the catatonia to depression, schizophrenia or an organic illness. The presence of prominent

* Corresponding author at: National Institute of Mental Health & Neurosciences (NIMHANS), Bangalore 560029, India.
E-mail address: urvakhsh@nimhans.ac.in (U.M. Mehta).

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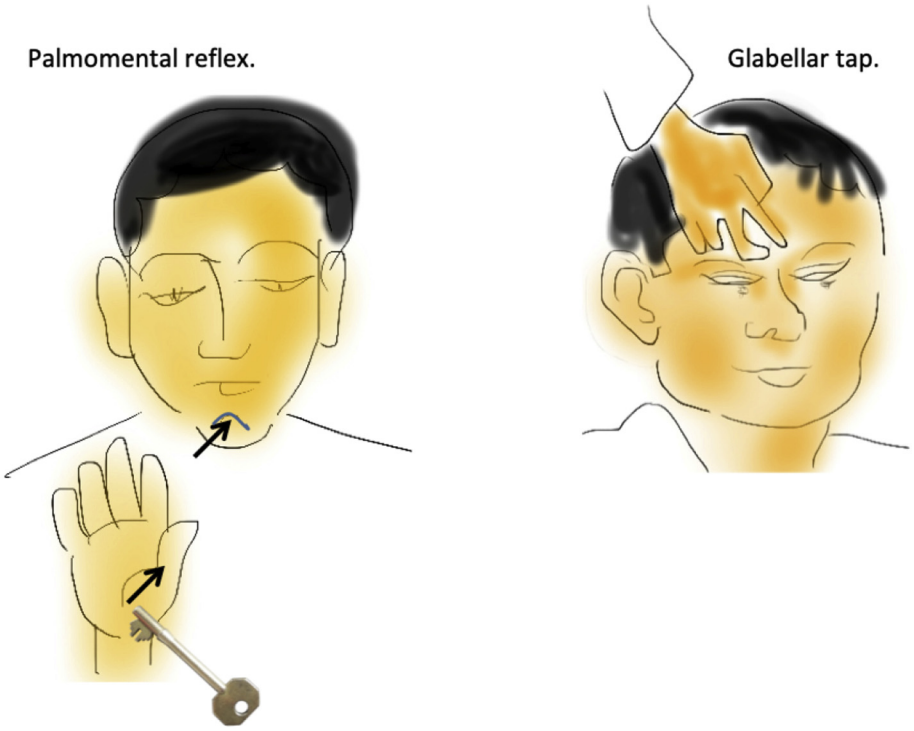

Fig. 1. Illustration of eliciting the palmomental and glabellar tap reflexes.

released reflexes (palmomental and glabellar tap) and an increased blink rate prompted the attending clinician (MSK) to treat her primarily as a case of schizophrenia. We prescribed oral trifluoperazine 20 mg/day, and she remained asymptomatic on this treatment for one year. Subsequently, she stopped medicines and came back for a consultation. During this visit, she had second and third person auditory hallucinations, delusions of reference, persecution and misinterpretation. There were no prominent mood symptoms elicited and she did not have any signs of catatonia. Over the next 35 years, she has had several (~15) psychotic exacerbations triggered by medication non-compliance, and her diagnosis was subsequently revised to paranoid schizophrenia (episodic course). The current exacerbation was over the last three months (in 2019, at age 63 years), after remaining asymptomatic and drug-free for the prior four years. Her current mental status examination also revealed multiple auditory hallucinations and delusion of persecution, but there was no evidence of primitive reflexes or an increased blink rate. She has now been initiated on oral risperidone 4 mg/day because of poor tolerability to trifluoperazine and chlorpromazine in the past, despite good response.

3. Discussion

This case illustrates the utility of palmomental reflex, glabellar tap and increased blink rate in predicting a possible diagnosis of schizophrenia (and thus selecting pharmacological treatment) in the absence of the typical schizophrenia symptoms – the clinical evaluation then had revealed only catatonic symptoms. The longitudinal course of symptoms described above, over the next 35 years validated the diagnosis of paranoid schizophrenia and treatment selection. This clinical judgment was perhaps a translational effect, shaped by then-contemporary research on 'soft' neurological signs (Keshavan et al., 1979) that had demonstrated substantially greater proportion of patients with schizophrenia (55%) to have a positive palmomental reflex as compared to patients with affective disorders (29%). Even though these three physical findings of palmomental reflex (Gupta et al., 1995; Keshavan et al., 1979), glabellar tap (Stevens, 1978) and increased blink rate (Karson et al., 1990) have been independently shown to be increased in untreated schizophrenia compared to healthy subjects, these signs are certainly not specific to this disorder. The absence of these signs in the current examination may reflect the possible effects of treatment since neurological soft signs have been reported to disappear with treatment (Emsley et al., 2017). While using these or other 'soft' neurological signs as sole markers of diagnosis or treatment is not going to yield good prediction models, they may be of value in corroborating diagnostic decisions when used in concert with other clinical data. These neurological signs may also assist in determining possible diagnosis and treatment selection in the absence of other reliable clinical signs or symptoms. Our report also highlights the importance of routinely conducting a physical and neurological examination in psychiatric patients (Sanders and Keshavan, 2002).

Contributions

MSK was the attending clinician of the patient in 1984 and made the clinical decisions. MSK also conceptualized the commentary/report, and edited the manuscript, prepared the figure. UMM was the attending clinician of the patient during follow-up in 2019. UMM performed the file review and drafted the manuscript. Both authors approve of the final version of the submitted manuscript.

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None.

Declaration of competing interest

Drs. MSK and UMM report no financial relationships with commercial interests.

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