Supplementary Note

On the issue of insight

Insight is a multidimensional construct with experiential (awareness), cognitive (attribution) as well as behavioural (acceptance) components[1]. The construct of loss of insight is defined on the basis of the pathological nature of delusions. Let us consider delusions to be on a mechanistic continuum with normal learning, i.e. associations formed at the synaptic level that are pathological *only because* they are maintained due to an inherent defect in homeostatic plasticity. Then the experiential aspect of a delusion must be the same as the experiential aspect of any associative learning. What sense of awareness regarding learned associations do we normally experience? While we can recall the content of learned material at will, the pairing (or binding) itself lacks an experiential component, irrespective of the strength of the paired stimuli. In other words, in terms of the aforementioned neural processes, a subject does not 'experience' the Hebbian processes in his/her conscious awareness, irrespective of its dose. By extension, no such awareness or insight can be expected for beliefs that are clinically identified as delusions. Thus, the lack of awareness as to the nature of the belief is likely to be the default state of delusions, irrespective of the diagnostic status of the individual.

But why should a patient with limited episodes of psychosis (delirium, ictal psychosis) have better insight than patients with schizophrenia? The aspect of insight that differs between these diagnostic groups is one of *attribution*, i.e. learning the association between the mental experiences and the illness construct. According to the inefficient system-stabilization model, the state of hyperconnectivity (figure 4) precludes the formation of new associations required for the correct attribution as well as for the extinction of established prior associations (delusions). As per the proposed theory, deterioration in the message-passing ability does not occur in individuals with intact functional plasticity (e.g. those with delirium or epilepsy). Thus, in the aftermath of a psychotic episode, patients with schizophrenia are less likely to make correct illness-related attributions.

When the structural homoeostatic compensation eventually succeeds in restoring message transmission (as shown in Figure 5), learning the association between the prior experience and the illness construct becomes more likely. In clinical practice, insight is often noted to improve after the initial episode[2,3], and relate to higher burden

of information processing deficits and psychomotor poverty[4], both being indicative of a shift in system-stabilization, as shown in figure 4.

Note that it is important to distinguish the awareness of the learning process from the awareness of the stimuli and the outcome of learning[5]. Associations can occur with or without the subject attending to a specific stimulus or an outcome[6]. For example, a depressed subject may selectively attend to negative words, increasing the probability that those stimuli get associated with innocuous bodily internal or external cues, though not being consciously aware of the process of 'binding'.

On bipolar disorder with psychosis

One of the limitations of this review is that it does not attempt to provide a unitary explanation to the heterogeneous symptoms seen in patients with all psychotic disorders. The extant literature on bipolar disorders has not been appraised in this regard.

Notwithstanding this, the description of temporary homeostatic overload (Figure 3) is likely to be relevant for the psychotic symptoms seen in mood disorders. Novel computational accounts of mood posit that mood states such as mania and depression are associated with abnormal synaptic receptor sensitivity, resistant to bottom up feedback[7,8]. This may increase the focus on sensory inputs that are presumed to be unpredictable, thus increasing the likelihood of associative plasticity that overloads the homeostatic capabilities, as long as the mood state persists. Nevertheless, in the absence of an inherent defect in homeostatic plasticity, the resulting psychotic symptoms resolve when the system-stabilization process eventually catches up. This means that psychotic symptoms always resolve when the mood state eases off in the case of bipolar disorder. The lack of such full resolution may indicate a certain degree of impairment in the topological homeostasis, clinically manifesting as schizoaffective illness.

Appendix 1 to Palaniyappan L. Inefficient neural system stabilization: a theory of spontaneous resolutions and recurrent relapses in psychosis. *J Psychiatry Neurosci* 2019.

Online appendices are unedited and posted as supplied by the authors.

1.   Amador XF, David AS. *Insight and psychosis: Awareness of illness in schizophrenia and related disorders, 2nd ed.* New York, NY, US: Oxford University Press; 2004.
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3.   Parellada M, Boada L, Fraguas D, et al. Trait and State Attributes of Insight in First Episodes of Early-Onset Schizophrenia and Other Psychoses: A 2-Year Longitudinal Study. *Schizophr Bull* [Internet] 2010 [cited 2010 Nov 30]; Available from: http://schizophreniabulletin.oxfordjournals.org/content/early/2010/09/30/schbul.sbq109.abstract
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6.   Field AP. I like it, but I'm not sure why: can evaluative conditioning occur without conscious awareness? *Conscious Cogn* 2000;9:13–36.
7.   Clark JE, Watson S, Friston KJ. What is mood? A computational perspective. *Psychol Med* 2018;48:2277–84.
8.   Chekroud AM. Unifying treatments for depression: an application of the Free Energy Principle. *Front Psychol* [Internet] 2015 [cited 2019 Feb 4];6. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4335302/