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Off to never-never land: losing consciousness to gain thought

In this issue of *Brain*, Smaranda Leu-Semenescu and colleagues describe one aspect of a rare and fascinating neuropsychological syndrome—auto-activation deficit (AAD)—in which patients with specific basal ganglia lesions experience an almost total loss of self-driven behaviour that can partially be reversed by external stimulation. Indeed, when questioned, some patients with AAD will consistently report a complete absence of spontaneous thoughts. For healthy individuals, spontaneous thoughts are not only a feature of waking life; they are also a common feature of that component of sleep that we call dreams. Leu-Semenescu and colleagues therefore asked whether the absence of mental content reported by patients with AAD also persisted during sleep—that is, are individuals with no spontaneous waking thoughts able to dream?

As described in their article, sleep stages were recorded from each of a group of 13 patients with AAD and a group of matched healthy controls using a combination of EEG and other physiological measures. During periods of both rapid eye movement (REM) and non-REM sleep, all participants were awoken and asked to report their mental contents immediately before waking. Surprisingly, despite reporting a total absence of mental content during wakefulness, some patients with AAD nevertheless reported dream contents, primarily during REM sleep. This intriguing dissociation raises many questions about the neural origins of dreams.

The authors ascribe their observations to a 'bottom-up' theory of dreaming in which, during REM sleep, random fluctuations in brainstem activity ascend to stimulate sensory cortical regions that may, in turn, evoke sensory dream contents in patients with AAD (Nir and Tononi, 2010). This interpretation, alongside the specific basal ganglia lesions of the patients, raises the question of what neural mechanisms are minimally sufficient to result in dreams. Indeed, could it be that other populations of severely brain-injured patients whose pathologies include a relative preservation of the brainstem—e.g. those in the vegetative and minimally conscious states (Adams *et al*., 1999)—may also experience dream content from a similar bottom-up mechanism? This is unlikely to be the case, as the patients with AAD exhibited broadly healthy sleep-architecture, while it is known that more diffuse forms of brain injury dramatically disrupt sleep/wake cycles (Cruse *et al*., 2013)—even entirely eliminating REM sleep (Landsness *et al*., 2011), the sleep stage in which the majority of dreams of the patients with AAD were reported.

Nevertheless, could the dream contents of the patients with AAD have come about as a result of a solely bottom-up mechanism? Despite reporting dreams upon awakening, there were marked qualitative differences when compared with healthy controls. Specifically, the dreams of patients with AAD were less complex, less bizarre and less emotional. The authors argue that, in healthy individuals, the more detailed and narrative aspects of dreams are the result of cortico-cortical interactions that 'clothe' the bottom-up random stimulations from the brainstem (Roffwarg *et al*., 1966). Indeed, theories of consciousness acknowledge the importance of long-range cortical connections for the experience of mental content (Tononi, 2004; Dehaene *et al*., 2006). REM sleep itself is also characterized by cortical effective connectivity that is akin to that seen during wakefulness (Massimini *et al*., 2010). It is therefore unclear how the hypothesized local activations elicited through brainstem stimulation alone would enter consciousness without some degree of cortico-cortical integration.

Due to the relative rarity of the syndrome, there is unfortunately a paucity of data describing the cortico-cortical connectivity of patients with AAD. In order to support their hypothesis, the authors cite prior work that shows a failure of patients with AAD to modulate their motor output in response to affective cues, despite retaining an ability to modulate the same motor output to command (Schmidt *et al*., 2007). The authors argue that this apparent disconnect between affect and action is indicative of an impairment of structural and/or functional connectivity in patients with AAD. Further complementary measures of structural and functional connectivity are required, however, in order to elucidate the relationship between cortico-cortical connections and the qualitative differences in the dreams of patients with AAD. For example, does diffusion tensor imaging reveal impairment in structural connectivity in the brains of patients with AAD, perhaps as

a result of atrophy down-stream of the basal ganglia lesions? Does resting-state functional MRI confirm the hypothesized impairments in functional connectivity during sleep and/or wakefulness?

The authors acknowledge that the bottom-up and top-down hypotheses of dream origin in healthy individuals are not mutually exclusive. Under these assumptions, therefore, it may be possible to investigate how these contents are differentially represented in the brain. Indeed, it has recently been shown that aspects of non-REM dream content may be decoded accurately from perceptual brain regions using functional MRI (Horikawa *et al*., 2013). If such an approach can be applied to REM sleep, it may be possible to identify qualitative differences in the neural representations of dream content in patients with AAD when compared with controls, thereby helping to characterize the nature of both the hypothesized bottom-up dreams, and the more complex top-down narratives of healthy dreaming.

Further neuroimaging investigations would also speak to the individual differences seen across the AAD patient group. Indeed, only 31% of patients with AAD reported dreams during REM sleep. From the reported data, there appear to be no differences in aetiology or pathology between dreamers and non-dreamers. However, further studies using *in vivo* measures of structural connectivity, such as diffusion tensor imaging, may illuminate this inconsistency. For instance, the bottom-up theory of dreaming, as expounded by the authors, would predict that there is a greater reduction in brainstem-to-cortex connectivity in non-dreamers that therefore leads to reduced stimulation of the cortex during REM sleep.

In summary, the article by Leu-Semenescu and colleagues provides a fascinating insight into a rare neuropsychological syndrome, while simultaneously serving to illustrate further how investigations of altered forms of consciousness—be it those caused by brain-injury, or by the simple onset of sleep—may provide us with unrivaled insights into consciousness itself, and how the brain supports our ongoing mental contents.

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Damian Cruse
Brain and Mind Institute,
Western University,
London, ON, Canada
E-mail: dcruse@uwo.ca

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