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Sleepy or Tired?

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I find the essay by Cirelli & Tononi about the essentiality of sleep highly enlightening in its systematic presentation and its comprehensive review of the pertinent literature.

Perhaps a weakness of the essay is the lack of definitions given for states that are regarded as closely related (sleep, quiet wakefulness, rest: p. 1608), and the states of wakefulness or sleep deprivation as a contrast to sleep when it comes to its cellular function (p. 1609). This shortcoming in my opinion relates to the lack of controlled conditions that still prevail in many sleep-related studies. The authors point out rightly that more future experiments should directly compare the restorative value of quiet wakefulness and sleep.

But even more interesting would be the differential effects of drugs on "sleepiness" versus "tiredness" (p. 1608) since they could more objectively probe the underlying systems than pure observations and still elicit behavioral reports. While the contrasting semantics of "sleepy" and "tired" may not be fully intuitive, the didactic association of the former with general arousal and sleep-promoting systems, and the latter with local cell groups whose function deteriorates likely as a sequel of metabolic wear-out, goes a long way. We should not forget though that the supposedly diffuse ascending systems have regional preferences (often for prefrontal cortex) and that the responsiveness of local cell groups to the associated neuromodulators may vary so that regional effects in PET studies of glucose metabolism may not uniquely indicate levels of "tiredness". Some drugs are of course designed to modulate "sleepiness" via ascending arousal systems, but can it be deduced that others that affect the ubiquitous GABAergic neurons, such as benzodiazepines and barbiturates, affect "tiredness"? And finally, why do anti-cancer treatments, such as radiotherapy, and most chemotherapeutics induce "fatigue"? This is yet another term that will have to be better defined in the future in terms of underlying mechanisms.