

individual neurons. In Parkinson's disease, the slow dancer inhibits the faster one from implementing his fancy footwork, therefore limiting their combined ability to generate movement itself (I'm sure some of us can relate). What this means physiologically is that enhanced coupling with prominent beta oscillations prevent higher frequency gamma oscillations in the motor cortex from encoding and ultimately directing appropriate movement.

By meticulously parsing out these distinct signals, the authors found that electrical stimulation deep in the STN uncouples the slow beta from fast gamma oscillations in the motor cortex, thereby reducing PAC both at rest and during volitional movement. More remarkably, the degree to which DBS elicited a reduction in oscillatory coupling was closely associated with improvement in certain motor symptoms, such as muscle rigidity. The authors also demonstrated that the temporal relation between PAC reduction and symptom improvement were closely linked. To further confirm that such reduction was not simply a result of wishful thinking by hypervigilant testers, the authors blinded the testers to whether and how much stimulation was being given. Finally, they considered other potential confounding factors, such as a simple reduction in the strength of beta oscillations. However, they observed that the association between slow and fast oscillations held across patients

and was largely preserved irrespective of the effect of stimulation on oscillatory strength.

Thus, like a good dance coach, DBS appears to disentangle the abnormal relationship between the slow and fast oscillations in the motor cortex. This reduction in coupling takes the brakes off the motor cortex, at least over the short timespans tested here, and allows neurons responsible for volitional motor control to generate movement. Moreover, this effect appears to be specific to these oscillatory couplings, which may be based, in part, on the particular connectivity of the STN within the motor system.

This study raises a number of intriguing questions. Although the authors demonstrate a striking correlation between DBS-related reduction in PAC and improvement in motor symptoms, this relation was not universal. For example, the ability of subjects to initiate movement did not appear to be highly correlated with the strength of PAC in the motor cortex, even though the ability to initiate movement is often prominently affected by DBS. One possible explanation for this is the type of behavioral test employed by the authors or area recorded. With some tweaking of the behavioral parameters, future investigation may provide additional understanding of how DBS exerts its effects. Further investigation may also aim to provide insight into how DBS improves parkinsonian symptoms in the long run, over months to years.

A second, related question is how to use this new insight to improve DBS treatment. For example, one may imagine recording from cortical sites in real time and using this information to intelligently guide the timing and frequency of DBS in deeper subcortical structures such as the STN. This idea of 'smart' closed-loop stimulation is rapidly evolving, and some pioneering teams, such as that of Hagai Bergman, are testing similar concepts in animals⁷. Rather than applying DBS indiscriminately, it may be possible to dynamically scan for enhanced PAC in the motor cortex. If and when such an event is observed or when the individual is planning to move, stimulation could be delivered in short, temporally focused bursts. With the fundamental insight provided by the present study, such prospective devices could potentially revolutionize the treatment of Parkinson's disease and related disorders.

COMPETING FINANCIAL INTERESTS

The author declares no competing financial interests.

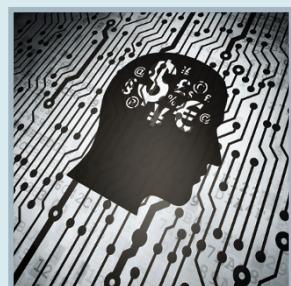
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The cost of brain structure

Experience alters brain structure and function—previous controlled studies have reported specific experience-dependent changes following training in sensory and motor tasks. Taking a step back, however, it is critical to understand how broader and less controlled influences and experiences affect the development of brain structure and function. Children from lower socioeconomic status (SES) families are known to be at a disadvantage in terms of educational and vocational achievement. Earlier studies have examined relationships between SES, characteristics of particular brain regions and cognitive skills. To date, none have looked at the influence of SES across the entire brain while accounting for genetic ancestry.

On page 773, Noble and colleagues investigated a diverse cohort of 1,099 children and adolescents from the United States, assessing whether parental education and family income, which contribute to SES, correlate with structural characteristics across the entire brain. After accounting for age and genetic ancestry, they found that parental education and family income had distinct associations with total surface area of a subset of frontal, temporal and parietal regions implicated in language and executive functions. Income uniquely accounted for the variance in surface area. Interestingly, a logarithmic relationship between income and total cortical surface area revealed that, at the lower end of the income scale, steeper increases in surface area were observed with small income increases. Surface area also partially mediated the association between income and performance in cognitive tasks.

These findings raise the possibility that interventions aimed at improving SES might positively affect cognitive function by influencing brain development, inviting a call to arms for immediate educational intervention for disadvantaged children. However, it must be noted that these findings do not demonstrate a direct causal relationship between SES and brain structure, nor do they suggest that this relationship is permanent. Additional factors can also contribute including stress, safety, nutrition and access to stimulating learning environments, and these data represent just one step forward in understanding how all of these influences affect brain development. Furthermore, similar analyses need to be performed on a more global scale, as each of these elements varies considerably across different countries. With these caveats in mind, we should recognize this study's importance in examining a subset of these broader influences on whole-brain development in a large cross-sectional cohort, and it will hopefully open the door for further studies and stimulate the development of interventional efforts to reduce SES disparities in cognitive development.



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