Motor Control: Exploring the Neurochemistry of Subliminal Inhibition

A new study links individual differences in unconsciously triggered motor control to variability in GABA neurotransmitter concentration in the supplementary motor area of the human brain.

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It has been known for some time that masked ‘prime’ stimuli, presented below the threshold of conscious perception, can bias behavioral responses to subsequent probe stimuli, facilitating prime-compatible and hindering prime-incompatible responses, presumably by partially activating prime-compatible motor pathways [1]. More recently, this picture has been qualified by the intriguing observation that, with certain prime-to-probe delays, this classic effect can be reversed, resulting in a ‘negative compatibility effect’ where the prime-compatible probe response is slowed [2]. This effect has been attributed to an unconscious act of motor control, consisting of the automatic inhibition of a partially activated response if it is no longer supported by unequivocal perceptual input [2,3].

The negative compatibility effect has attracted much attention [4,5], for several reasons. First, the very notion of unconscious or automatic ‘control’ sets the pulses of cognitive psychologists racing, because it represents an oxymoron vis-à-vis the traditional view of control processes being, by definition, volitional and effortful [6,7]. In fact, in combination with other recent work on seemingly ‘automatic’ strategic control [8–11], research employing the negative compatibility effect has contributed forcefully to the ongoing erosion of the traditional dichotomy between ‘automatic’ and ‘controlled’ processing [12,13].

Second, if the negative compatibility effect were an unconscious automatic mechanism, and was thus presumably immune to the noisy caprice of volitional processes, it could potentially serve as an attractive measure of individual differences in inhibitory control in the clinical domain [14,15]. On both counts, a thorough understanding of the neural mechanisms underlying the negative compatibility effect would be of great interest.

In this issue of Current Biology, Boy and colleagues [16] make an enlightening contribution to this quest, by harnessing an innovative combination of behavioral and neuroimaging techniques. Previous lesion data had implicated the supplementary motor area (SMA) as a key region in producing the negative compatibility effect [17]. Armed with these data, the authors set out to ask what, in this field, is a highly important, but rarely posed, question: can individual differences in behavior be explained by regionally specific variability in neurochemistry? And specifically, might individual differences in the expression of subliminal motor control be related to variability in the concentration of the brain’s primary inhibitory neurotransmitter, gamma-aminobutyric acid (GABA), in the SMA? Boy et al. [16] pursued this question by combining careful behavioral experimentation with magnetic resonance spectroscopy (MRS), an imaging technique that exploits the fact that different metabolites in the brain have different resonant frequencies, thus producing MR spectra with peaks that reflect the relative concentration of different molecules, including the neurotransmitters glutamate and GABA [18].

Boy et al. [16] first established that the negative compatibility effect represents a stable, trait-like measure, displaying high test-retest reliability within individuals. Subsequently, they employed structural magnetic resonance imaging (MRI) for anatomicall y localizing the SMA in each participant, in order to then acquire MRS data from a cortical volume centered on this area. Finally, the quantification of the area under the GABA peak in each individual’s MR spectrum enabled Boy and colleagues to assess the relationship between individual differences in SMA GABA concentration and subliminal motor inhibition, as gauged by the negative compatibility effect. The results indicated a strong inverse relationship, which proved to be robust across two independent subject cohorts. Importantly, this correlation between GABA and automatic motor control was regionally specific: MRS data collected from a number of control regions that are associated with various forms of action control, including the anterior cingulate, dorsolateral prefrontal cortex, parietal cortex, and inferior frontal gyrus, all yielded null results. Similarly, the association between SMA GABA...
concentration and negative compatibility effect magnitude was also found to display functional specificity, in that it neither extended to global reaction time measures, nor to other types of motor control as assayed by a range of comparison tasks, including the Simon, flanker, and stop tasks [16].

Two aspects of these data are particularly noteworthy. First, the results obviously answer the experimental question in the affirmative, in that individual differences in GABA concentration in the SMA appear to be a crucial determinant of inter-individual variability in the strength of automatic response inhibition. This result is evidently of interest for understanding the negative compatibility effect phenomenon per se but, importantly, it should also foster more general excitement, as it is a fine demonstration of the feasibility of adding MRS to the basic toolkit of the cognitive neuroscientist. Whereas much fanfare has surrounded recent progress in linking functional genetic polymorphisms to individual differences in functional MRI measures and behavior [19], attempts to link MRS-afforded regionally specific measures of (in large part genetically driven) neurotransmitter expression with behavioral probes of discrete cognitive function have been comparably neglected. The current observation [16] of a surprisingly tight coupling between behavior and MRS measures (see also [20]) should provide additional motivation for the quest of ultimately bridging genetic polymorphisms to regionally specific metabolite density, to regional functional MRI responses, to behavior. An unfortunate dampener for this endeavor, however, is the fact that key neurotransmitters like dopamine, serotonin, and acetylcholine at present appear to be invisible to MRS, perhaps because of their low concentrations.

The second intriguing feature of Boy et al.’s [16] results is the direction of the association between SMA GABA concentration and the negative compatibility effect. Intuitively, this relationship could perhaps be expected to be positive, with more GABA equating with more motor inhibition, but the opposite was in fact the case: subjects with higher GABA concentration in their SMA displayed smaller negative compatibility effect magnitudes. This suggests that the SMA itself is not the target site of automatic motor inhibition, that is, where the partial response preparation is being suppressed, but rather that it acts as the source of the inhibitory brake, initiating the response inhibition that is ultimately carried out elsewhere, in all likelihood, the basal ganglia [14,15]. This role for the SMA fits well with previous lesion data showing an absence (rather than amplification) of the negative compatibility effect in a rare patient with an exclusive SMA lesion [17]. Furthermore, this finding is important because it highlights the capability of MRS-derived measures to not only speak to regional neurochemistry itself, but to help adjudicate between rival functional hypotheses regarding the role of a particular brain region in a particular cognitive process.

Naturally, these results also inspire questions for future research. For instance, the reported lack of associations between SMA GABA concentration and a range of tasks invoking motor control processes other than the unconscious inhibition reflected in the negative compatibility effect raises the issue as to what factors exactly differentiate these types of motor control, and, by extension, what best characterizes the response control processes mediated by the SMA, as opposed to, for example, the pre-SMA, or the basal ganglia. A priori, it appears unlikely that the subliminal nature of the control trigger would constitute the crucial distinguishing feature, but a definitive answer to this question will clearly have to await additional empirical work. The type of innovative experimental approach pursued by Boy and colleagues [16] seems well-suited to address these issues, as well as to encourage other researchers to take a hitherto rarely traveled road and start bridging the gap between well-defined cognitive-behavioral phenomena and regionally specific neurochemistry.

References

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