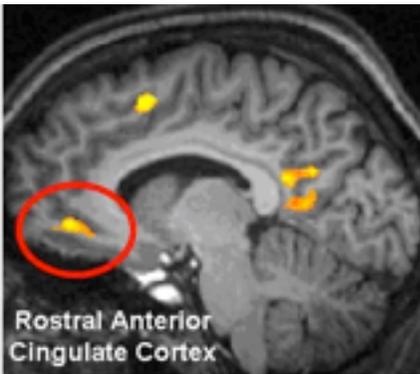


# NEW FINDINGS IN DEPRESSION

## Neuroimaging Predictors of Treatment Response in Depression

*From presentations by Dr. Diego Pizzagalli & Dr. Jonathan Downar at the CANMAT Mood & Brain conference, 2014*

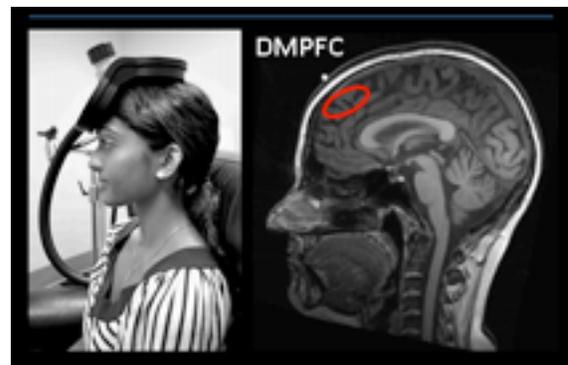
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To date, no single clinical variable has been identified as an adequate predictor of treatment outcome for Major Depressive Disorder (MDD). This has prompted researchers to explore biomarkers of treatment response, which could guide therapy selection and development. At the CANMAT conference on January 25th, 2014, Dr. Diego Pizzagalli and Dr. Jonathan Downar presented on the current state of neuroimaging biomarkers of response in MDD.

One brain area that has demonstrated consistent dysfunction in depression is the rostral anterior cingulate cortex (rACC) in the frontal lobe. This brain area interacts with other frontal and limbic brain regions that are together important for emotional regulation and cognitive control. Dr.

Pizzagalli reported that high pre-treatment activity in this area is predictive of antidepressant response months later (Pizzagalli et al, 2001), a finding that has been replicated across antidepressants (Korb et al, 2009; Pizzagalli et al, 2011). However, this effect was not observed for cognitive behavioural therapy, suggesting the rACC has modality specific effects. Furthermore, these findings have implications with respect to developing novel interventions. Cognitive training targeting specific brain areas has emerged as a potential therapy for depression. In a small proof-of-



concept study in healthy controls evaluating cognitive training targeting the rACC over 5 days, participants demonstrated improved reaction times and conflict monitoring in addition to increased activity in the rACC and dorsolateral prefrontal cortex (Millner et al, 2012).

Another example of how biomarkers of depression can guide treatment is with repetitive transcranial stimulation (rTMS). Typically, the brain target for stimulation is the dorsolateral prefrontal cortex. However, Dr. Downar proposes that the dorsomedial prefrontal cortex (DMPFC) may be a more effective target. This is based on findings that the DMPFC, which is important for self-control and affect regulation (Sheline et al, 2010), is reduced in size among depressed individuals (Bora et al, 2012). Volume decreases in this area are consistent with the difficulty experienced by MDD patients in regulating thoughts.

Since 2010, DMPFC stimulation has been conducted in the rTMS clinic at University Health Network. Interestingly, responders began with low connectivity, which increased post-treatment, between the DMPFC and other areas of the brain that are important for reward response (Downar et al, 2014). Integrating clinical features into this model supported these findings, where loss of pleasure and pessimism were the only variables to distinguish responders from non-responders (responders were less likely to report these symptoms). In other words, the responders had an intact reward circuit similar to healthy controls and the non-responders did not. Importantly, half of the patient sample still does not improve with rTMS; thus, robust biomarkers are needed to distinguish responders pre-treatment.

While the use of neurobiological tools to identify biomarkers may prove to be a fruitful endeavor, these biomarkers need to be based in clinical phenotypes in order to have face validity. Therefore, the future of biomarker research should focus on integrating clinical, neuroimaging as well as genetic/molecular information in order to develop an algorithm to predict treatment response.

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