1	Decentering mediates the relationship between vmPFC activation during a stressor and
2	positive emotion during stress recovery
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## 21 Abstract

The stress response has profound implications on health and behaviour and stress is considered a risk factor for the development of psychopathologies including depression. The neural mechanisms supporting successful stress recovery are not fully understood, however a novel study by Yang et al. demonstrates that vmPFC activation during a stressor is related to improved stress recovery, and that decentering is able to mediate this relationship, suggesting a role during stress recovery. It was also revealed that vmPFC activation at different time points during the stressor predicts altering aspects of stress recovery, an observation that was only possible due to the adoption of change-point analysis.

29 The World Health Organization has cited stress as the health epidemic of the 21<sup>st</sup> Century. The ability 30 to respond to life's stressors has important implications for physical and mental health; stress is the 31 most common risk factor for developing mood disorders including major depressive disorder (MDD; 32 Risch et al., 2009), and the regulation of emotion has been shown to play an important role in protecting individuals from developing various psychopathologies including substance-related disorders, anxiety 33 34 and depression (Aldao, Nolen-Hoeksema, & Schweizer, 2010). Additionally, regulation of both negative emotion and positive emotion are important features of the stress response. One mechanism 35 through which positive emotion is able to impact stress is by facilitating stress recovery (Waugh, 36 Hamilton, Chen, Joormann, & Gotlib, 2012). Consequently, understanding the neurobiology 37 underpinning successful stress recovery, alongside factors that mitigate stress recovery, will aid in the 38 39 development of treatments and interventions concerned with improving individuals' physical and mental health. 40

Greater cognitive resource availability during stress recovery may aid successful deployment of stress regulation strategies such as decentering, a meta-cognitive strategy enabling one to modify their experience from within one's subjective experience onto that experience, and viewing one's experiences in a more objective manner. Bernstein et al's. (2015) metacognitive processes model of decentering includes three interrelated processes; meta-awareness, disidentification from internal experience, and reduced reactivity to thought content. Prefrontal cortex (PFC) brain regions underpin cognitive processes involved in top-down control of emotion, as well as subcortical affective structures.

48 The dorsolateral prefrontal cortex (dlPFC), ventrolateral prefrontal cortex (vlPFC), and dorsal anterior cingulate cortex (dACC) are involved in top-down regulation of emotion, and have been shown to 49 50 moderate activity in subcortical systems (e.g. the amygdala) underpinning affective reactivity (Ochsner, 51 Silvers, & Buhle, 2012). Whilst there is no direct anatomical pathway connecting the dIPFC and the 52 amygdala (Ray & Zald, 2012), it has been suggested that the dACC may serve as a mediation hub, allowing the dlPFC to exert an indirect influence on amygdala response (Ochsner et al., 2012). It has 53 54 also been hypothesized that the vmPFC, which provides information about positive emotion and whose activity is positively correlated with PFC activation and negatively correlated with amygdala activation 55 56 during emotion regulation (Ochsner et al., 2012), may act as a mediator within the dlPFC-amygdala pathway due to its anatomical connections with the amygdala and PFC regions (Ray & Zald, 2012). 57 Although progress has been made advancing understanding of the role positive emotion has during 58 59 stress recovery, the neural mechanisms supporting this are still poorly understood. A novel study by Yang et al. (2018) investigated the neural mechanisms underpinning the role of positive emotions 60 during stress recovery. The authors tested the proposal that the vmPFC acts as a hub via which positive 61 62 emotion influences stress recovery through the dlPFC-dACC-amygdala pathway, and additionally 63 whether decentering can mitigate stress recovery.

Yang et al. required participants to complete a stressful anagram task whilst neural activation 64 65 was recorded with functional magnetic resonance imaging (fMRI). Prior to the main experimental data 66 collection session, participants were trained to use emotion rating scales, and practiced an easy version of the anagram task. Subsequently, participants completed a stressful anagram task containing 15 67 anagrams of which 5 were easy, 5 were difficult, and 5 were unsolvable. Participants viewed the 68 69 anagrams for 4 seconds followed by a 5 second period in which they were required to solve the anagram 70 and provide their answer on a keypad. Participants were provided with immediate feedback, however this feedback included artificially inflated scores with respect to other participants' performance. The 71 stressful anagram task lasted for 3 minutes and upon completion participants viewed their overall 72 performance alongside a comment stating that '73% of participants performed better than them'. 73 74 Subsequently, individuals rated their emotion and then immediately began a 3 minute post-stressor

75 recovery period during which they were asked to think about the anagram task and to engage in any 76 thoughts and feelings that come naturally, whilst simultaneously watching either a positive or neutral 77 video. Participants rated their emotions before the anagram task (baseline), after the anagram task (post-78 stressor), and after emotion induction (recovery); consisting of a positive emotion question (how 79 pleasant do you feel right now?), and a negative emotion question (how unpleasant do you feel right 80 now?). Responses were made on a 5-point scale with 0.5 increments. Next, participants completed a 5-81 point decentering questionnaire providing state measures of rumination and decentering (e.g. I had the sense that I was fully aware of what was going on around me and inside me). Finally, participants 82 completed a post-task thought content questionnaire that asked questions relating to positive, negative, 83 84 or irrelevant thoughts and feelings about the stressor (anagram task) and video. All statements (e.g. I thought that the video was calming) were presented on a 5-point scale. The fMRI analytical technique 85 86 adopted change-point analysis to allow the identification of brain regions responsive to the stressor and recovery tasks. Yang et al. state that this approach provides a model-free method of detecting when and 87 for how long anatomical regions are active during a given experimental session, enabling the 88 identification of multiple activation peaks. Such analysis is not possible using traditional general linear 89 90 modelling which is not designed to detect the precise timing or duration of changes in physiological data or psychological events. Change-point analysis permits researchers to map precisely when during 91 92 an experimental protocol (e.g. the exact time during a stressor) hypothesized activation occurs, and this 93 can be mapped to corresponding behavioural measures (e.g. self-reported stress recovery).

94 Yang et al. demonstrated that during the stressful anagram task, increased neural activation in medial frontal cortex regions including the vmPFC, dorsomedial prefrontal cortex (dmPFC) and 95 anterior cingulate cortex were related to higher reported positive emotion during recovery. Importantly, 96 97 this relationship was only evident for individuals reporting high levels of positive emotion (compared to low levels of positive emotion) during stress recovery. Secondary mediation analysis focussing on 98 the vmPFC was carried out on an a priori basis. This approach revealed vmPFC activation during the 99 stressor did not directly predict negative emotional recovery. However, the indirect path between 100 101 vmPFC activation and negative emotional recovery via positive emotional recovery was significant,

102 suggesting that increased vmPFC activation during the stressor predicted increased positive emotional 103 recovery, and this association in turn improved negative emotional recovery. Exploratory analysis 104 investigating possible relationships between vmPFC activation and stress reactivity demonstrated that 105 overall vmPFC activation during the stressor was not related to emotional stress reactivity. However, 106 when neural activation of the vmPFC during the stressor was investigated temporally, two differing 107 relationships emerged in relation to stress reactivity. During the first half of the stressful anagram task increased vmPFC activity was associated with greater negative emotional reactivity, whereas during 108 the middle portion of the stressor vmPFC activation was related to increased positive emotional 109 recovery. This observation may represent a normal response profile to stress with early vmPFC 110 activation indicative of an evaluation that the stressor is negative. Sustained vmPFC activity during the 111 112 middle portion of the stressor, which is correlated with positive emotion recovery, may be reflective of 113 successful regulation of the stressor. These findings suggest temporal differences in vmPFC activation during the stressor were related to different aspects of emotional recovery and demonstrate the 114 advantage of employing a change-point analysis framework that allows temporal neural dynamics to be 115 investigated. In clinical populations less effective at regulating stress recovery, and less likely to 116 117 demonstrate typical vmPFC recruitment during stressful tasks, longitudinal research will be able to elucidate whether changes in vmPFC structural connectivity and functional activity are related to both 118 119 clinical improvements in stress regulation and increased use of decentering.

120 To investigate individual difference traits that may moderate biobehavioral indices during stress and subsequent emotional recovery, trait levels of decentering were recorded. Decentering was 121 positively correlated with vmPFC activation. Further, decentering was shown to mediate the 122 relationship between positive emotional recovery and vmPFC activity, whereas the direct relationship 123 124 between vmPFC activity and positive emotional recovery was non-significant. Taken together, these results provide novel evidence that vmPFC activation during a stressor impacts positive emotion and 125 provides benefits on stress regulation not seen until recovery. Further, decentering was shown to 126 127 mediate the relationship between vmPFC activation and positive emotion during stress recovery suggesting that decentering is important for successful stress recovery. 128

Although not discussed by Yang et al., decentering has recently become the focus of clinical 129 research aimed at improving therapies for anxiety and depressive disorders. Psychiatric disorders 130 131 including generalised anxiety disorder (GAD) and MDD are often characterized by reduced trait levels of decentering and altered activation of the default network (DN), comprising the medial prefrontal 132 133 cortex and posterior cingulate cortex. Decentering is also associated with activation of these brain regions, and altered resting state activity in the DN system is observed in GAD and MDD, whilst 134 associations in intrinsic functional connectivity of the DN have been observed as a function of changes 135 in decentering (Fresco et al., 2017). Further, emotion regulation therapy, a theoretically derived and 136 mechanistic focussed treatment targeting the normalization of biobehavioral deficits, has demonstrated 137 reductions in GAD and MDD severity alongside clinical improvements in decentering (Renna et al., 138 2018). Yang et al. build upon these findings showing that decentering can mediate the relationship 139 140 between activation of the vmPFC during a stressor and subsequent emotional recovery, and suggests that decentering should be included in biobehavioral models of stress recovery. 141

### 142 Future directions

143 It has been recommended that both positive and negative emotion conditions are included within affective neuroscience study designs (Bendall, Eachus, & Thompson, 2016). Such an approach permits 144 researchers to make more precise interpretations regarding the neurocognitive mechanisms 145 146 underpinning affective processing. For instance, without a negative emotion condition included within a study design, authors may suggest any observed differences in neurocognitive indices between 147 positive and neutral conditions are specific to the positive condition. However, it is possible that in 148 some situations such an interpretation may not be the most appropriate with results instead reflecting a 149 more general impact of valence. For example, brain regions including the amygdala, ventral striatum, 150 dmPFC, and vIPFC have demonstrated increased activation in relation to positive valence and negative 151 152 valence (Lindquist, Satpute, Wager, Weber, & Barrett, 2016). Theoretical work also supports inclusion 153 of both positive and negative emotion conditions. Yang et al. briefly discuss the broaden-and-build 154 theory (Fredrickson, 2001) and provide a valid theoretical rationale as to why positive emotion may 155 facilitate stress recovery (via positive emotions broadening of attention). However, the broaden-and-

build theory also makes predictions regarding the impact of negative emotion on behaviour – predicting
they have the opposite effect (a narrowing of attentional focus and reduction in cognitive resources).
Future studies aimed at investigating the role of emotion on stress recovery should adopt positive
emotion and negative emotion conditions, as well as neutral control conditions.

Self-report questionnaires are often adopted in affective neuroscience study designs. Whilst this 160 approach provides one method of recording affective information there known limitations in self-report 161 162 data (e.g. socially desirable responding). Indeed, Yang et al. acknowledge that future research would benefit from adopting more objective physiological indices of stress response (e.g., cortisol sampling 163 to assess hypothalamic-pituitary-adrenal axis activity). Cardiovascular recovery following a stressful 164 task has been investigated with results indicating blood pressure recovery was impeded by both negative 165 166 emotion and rumination (repetitive and intrusive negatively-focused and unconstructive thought), but was not enhanced by positive emotion (Radstaak, Geurts, Brosschot, Cillessen, & Kompier, 2011). A 167 significant correlation between rumination and negative emotion recovery is observed by Yang et al., 168 indicating that greater rumination led to less recovery, though no further exploration of this maladaptive 169 170 coping strategy appears to have been conducted. Rumination has been related to a number of psychopathologies, including MDD, as well as to negative-valence-specific biases in attentional control 171 that are associated with impaired inhibition and cognitive control (Koster, De Lissnyder, Derakshan, & 172 173 De Raedt, 2011), reinforcing the need to consider valence-specific effects alongside both adaptive and 174 maladaptive coping strategies.

Future research should investigate the neurocognitive mechanisms underpinning beliefs about stress. Perception of relative stress harm has been shown to influence mortality rates where individuals who report higher levels of stress and believe that stress negatively impacts health suffer from increased risk of premature death (Keller et al., 2012). Such research would benefit from adopting longitudinal anatomical and functional neuroscientific approaches that permit the investigation of changes in brain morphology, structural connectivity and neural activity with respect to stress recovery and the mediating role of individual difference traits such as decentering. 182 Adopting an elegant and rigorous study design Yang et al. provide novel insights relevant to biobehavioral models of stress recovery and positive emotion demonstrating that decentering can 183 mediate the relationship between vmPFC activation during a stressor and subsequent emotional 184 recovery. The adoption of change-point analysis allowing temporal neural dynamics to be investigated 185 186 revealed multiple vmPFC activity peaks during a stressor and these predicted different aspects of stress recovery. Research building upon these correlational findings adopting experimental manipulations is 187 required to allow causal interpretations to be made. Such research will help to reveal the neurocognitive 188 mechanisms underpinning successful stress recovery and should provide valuable insight to those 189 wishing to develop evidence-based translational therapeutic interventions. 190

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242