

with greater mortality after acute ischemic stroke ( $p=0.0002$ ). Nonetheless, abnormal BPC was not associated with degree of impairment ( $p=0.3734$ ), degree of disability ( $p=0.684$ ), or length of stay (LOS) in the acute stroke care center ( $p=0.9541$ ) after adjustment for major potential confounders. *Conclusions:* In patients with acute ischemic stroke, thrombocytopenia and thrombocytosis on the initial admission is associated with higher mortality after stroke. Abnormal BPC does not adversely affect the degree of impairment and disability, or LOS in the acute care center after acute ischemic stroke.

## E.02

### Arterial tortuosity: an imaging biomarker of childhood stroke pathogenesis?

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*Background:* Arteriopathy causes most childhood arterial ischemic stroke (AIS). Mechanisms are poorly understood but may include abnormalities of arterial structure. Extracranial dissection is common while intracranial dissection may explain idiopathic focal cerebral arteriopathy (FCA). We aimed to quantify cerebral arterial tortuosity and hypothesized increased tortuosity in extracranial dissection. *Methods:* Children with AIS were recruited within the Vascular-Effects-of-Infection-in-Pediatric-Stroke (VIPS) study (controls from the Calgary Pediatric Stroke Program). A validated software method calculated mean tortuosity of major cerebral arteries using 3D time-of-flight MR angiography (MRA). Blinded, multi-investigator reviews defined diagnostic categories. Tortuosity was compared between dissection (spontaneous and traumatic), FCA, moyamoya, meningitis, and cardioembolic, and controls (ANOVA, post-hoc Tukey). *Results:* A total of 116 children were studied. Age and gender were comparable across groups. Tortuosity scores and variances were consistent with validation studies. Tortuosity in controls ( $1.333\pm 0.039$ ,  $n=15$ ) was comparable to moyamoya ( $1.324\pm 0.038$ ,  $p=0.99$ ,  $n=15$ ), meningitis ( $1.348\pm 0.052$ ,  $p=0.98$ ,  $n=12$ ) and cardioembolic ( $1.379\pm 0.056$ ,  $p=0.19$ ,  $n=27$ ) cases. Tortuosity was higher in dissection ( $1.398\pm 0.072$ ,  $p=0.02$ ,  $n=22$ ) and FCA ( $1.421\pm 0.076$ ,  $p=0.001$ ,  $n=25$ ). Traumatic ( $1.391\pm 0.036$ ,  $n=9$ ) and non-traumatic ( $1.403\pm 0.090$ ,  $p=0.671$ ,  $n=13$ ) scores were not different. *Conclusion:* Children with dissection have more tortuous arteries. Quantified tortuosity may represent a clinically relevant biomarker of vascular biology in pediatric stroke.

## E.03

### Dorsal striatum mediates cognitive control, not cognitive effort per se, in decision-making: an event-related fMRI study

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*Background:* Whether the dorsal striatum (DS) mediates cognitive control or cognitive effort per se in decision-making is unclear because as cognitive control requirements of a task intensify, cognitive effort requirements increase proportionately. We implemented a task that disentangled cognitive control and cognitive effort to

specify the function DS mediates in decision-making. *Methods:* Sixteen healthy young adults completed a number Stroop task with simultaneous blood-oxygenation-level-dependent response (BOLD) measurement. Participants selected the physically larger number of a pair. Discriminating smaller physical size differences increases cognitive effort, but does not demand greater cognitive control. We also investigated the effect of interdimensional conflict between physical size and numerical magnitude. Selections in this incongruent case are more cognitively effortful and require greater cognitive control to suppress responding to the irrelevant dimension. Enhancing cognitive effort or cognitive control requirements increases response times and error rates. *Results:* Behavioural interference occurred for both conditions; however, DS BOLD signal only correlated with interference due to increased cognitive control requirements. DS was not preferentially activated for discriminations of smaller relative to larger physical size differences between number pairs, even when using liberal statistical criteria. *Conclusions:* Our findings support the increasingly accepted notion that DS mediates cognitive control specifically and does not index cognitive effort per se.

## E.04

### Design and development of drugs for Alzheimer's dementia as a protein misfolding disorder

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*Background:* There are no disease modifying agents for the treatment of Alzheimer's disease (AD). Pathologically, AD is associated with the misfolding of two peptides: beta-amyloid (plaques) and tau (tangles). *Methods:* Using large-scale computer simulations, we modelled the misfolding of both beta-amyloid and tau, identifying a common conformational motif (CCM; i.e. an abnormal peptide shape), present in both beta-amyloid and tau, that promotes their misfolding. We screened a library of 11.8 million compounds against this in silico model of protein misfolding, identifying three novel molecular classes of putative therapeutics as anti-protein misfolding agents. We synthesized approximately 400 new chemical entity drug-like molecules in each of these three classes (i.e. 1200 potential drug candidates). These were comprehensively screened in a battery of five in vitro protein oligomerization assays. Selected compounds were next evaluated in the APP/PS1 doubly transgenic mouse model of AD. *Results:* Two new classes of molecules were identified with the ability to block the oligomerization of both beta-amyloid and tau. These compounds are drug-like with good pharmacokinetic properties and are brain-penetrant. They exhibit excellent efficacy in transgenic mouse models. *Conclusion:* Computer aided drug design has enabled the discovery of novel drug-like molecules able to inhibit both tau and beta-amyloid misfolding.