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Non Animal Alternatives for Studying Attention and Attentional Deficits in Humans

I. Neuroimaging Techniques

Neuroimaging techniques—including high-resolution anatomical neuroimaging (MRI),[1] functional neuroimaging (fMRI),[2] single photon emission computed tomography (SPECT),[3] diffusion tensor imaging (DTI),[4] positron emission tomography (PET),[5] transcranial magnetic stimulation (TMS),[6] electroencephalography (EEG),[7] and magnetoencephalography (MEG)[8]—are advancing our understanding of the neural underpinnings of visual, spatial, and auditory attention; stimulus selection; and disordered attentional processes in humans. It is data from these non-animal research studies that have paved the way for the current pharmaceutical, behavioral, and TMS-based treatments currently used to treat attention deficit disorder (ADD) and that will continue to pave the way for safe, more effective treatments in the future.

Several research groups are also successfully combining the use of the tools described below to develop a comprehensive understanding of the complex interplay of structural, neurochemical, and electrophysiological mechanisms in typical and atypical human attention networks.[9,10,11,12,13,14,15,16,17,18]

a. fMRI/MRI/DTI

High-resolution fMRI has allowed researchers to study the neural networks involved in a variety of attentional mechanisms in humans performing species-relevant attention-mediated tasks,[19] including those requiring sustained attention,[20,21,22,23] attention-shifting,[24,25,26,27] selective attention,[28,29] and distraction-laden target selection[30,31] across and within stimulus modalities. These studies have also successfully deciphered the roles of the superior and inferior colliculi and lateral geniculate nucleus during visual, spatial, and auditory attentional processing in humans[32,33,34,35,36,37,38] and their interactions with cortical regions during that processing.[39,40,41,42]

Structural imaging tools, including high-resolution MRI and DTI, have been used to identify neurological abnormalities associated with ADD,[43,44,45,46] and fMRI has also been used to identify atypical activity within brain regions during impaired attentional processing in individuals with ADD.[47,48,49,50,51,52] These neuroimaging methods have been used to identify biomarkers for more accurate diagnosis of ADD[53,54] as well as to clarify the genetic[55,56,57,58] and environmental[59,60,61] contributors to ADD. These tools also allow researchers to study the variability in symptoms[62,63,64] and the impact of different treatments[65,66,67] in this population at the neurological level.

b. TMS

TMS in humans, which can be used to modulate neural activity in a target brain region, can now simulate the chemical lesion and induced activation and deactivation studies once performed on animals. This tool has been used extensively to detail the various roles of individual neural regions in the attentional networks in humans[68,69,70,71,72,73,74,75] and to systematically identify the functional and dysfunctional components of attentional networks in individuals with ADD.[76] Importantly, these investigations have led to the use of repeated TMS (rTMS) in healthy individuals and individuals with ADD as a successful method for improving attentional control.[77,78,79]

c. MEG/EEG

The ability to measure and localize electrophysiological responses in humans using EEG and MEG has provided researchers with an in-depth understanding of the time course of different neural contributions to attentional processes as well as the multi-mechanistic nature of human attention[80,81,82,83] These tools identified specific atypicalities in the ADD brain during a multitude of attention-related tasks that can be used for better diagnosis and potentially for the development of new treatments.[84,85,86,87]

d. PET/SPECT

PET and SPECT imaging allows researchers to determine the dopaminergic, serotonergic, nicotinergic, GABAergic, and noradrenergic systems in typical and atypical neurological functions. These methods have been used to pinpoint both the neuroanatomical and neurochemical contributors to attentional processes in humans.[88,89,90] Additionally, these tools have been used to successfully identify the neural correlates of individual variation within the ADD population.[91,92,93] PET and SPECT have been used to determine the dopaminergic,[94,95,96,97] noradrenergic,[98,99] GABAergic,[100] and serotonergic[101,102] dysregulation associated with ADD and to study the effects of pharmaceutical treatment on these systems in individuals with ADD.[103,104]

II. Computational Models of Attention

Computational and mathematical models have been instrumental in furthering our understanding of visual attention. There are numerous models that assist in clarifying and investigating theories of visual attention using human-relevant tasks and situations. These computational models fall into two broad categories: those that investigate bottom-up visual attention, which is driven by visual input and saliency and occurs rapidly, and those that model top-down attention, which is task-oriented, based on subjective experience, and goal-oriented.[105] Studies using computational modeling have successfully described how information from tasks such as making a sandwich guides eye movements[106] and how distractions while driving can affect eye movements,[107] as well as other human-relevant tasks and functions. Population receptive field (pRF) computational models have successfully mapped how clinical conditions such as autism and Alzheimer's can affect attentional networks and plasticity in the visual cortex.[108]

These tools have also been invaluable in elucidating the complex interactions between cortical and subcortical interactions during auditory and visual stimulus selection in humans[109,110,111,112] and in modeling aberrant information processing in ADD.[113,114,115]

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