The neural basis of stop-signal inhibition in healthy individuals and in schizophrenia patients

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Glossary of abbreviations

AAL……automated anatomical labeling
ACC……anterior cingulate cortex
ADJAR……..adjacent response technique
ADHD……attention deficit hyperactivity disorder
BA……..Brodmann Area
BOLD……blood oxygenation level dependent
DBS……deep brain stimulation
DLPFC……...dorsolateral prefrontal cortex
DSM……...Diagnostic and Statistical Manual of Mental Disorders
EEG……electroencephalogram
EOS……early onset schizophrenia
EPI……..echo-planar imaging
EPS…….extra-pyramidal symptoms
ERP…….event-related potential
FEF…….frontal eye fields
fMRI……...functional magnetic resonance imaging
FWHM……full width at the half-maximum
GABA…….gamma amino butyric acid
GABAergic…….using GABA as a neurotransmitter
GLM……...general linear model
GoRT……median Go reaction time
GP……...globus pallidus
GPe……..globus pallidus (*pars externa* - external capsule)
GPi……..globus pallidus (*pars interna* - internal capsule)
HRF…….....hemodynamic response function
IFG……..inferior frontal gyrus
IPL……..inferior parietal lobe
ISI……...interstimulus interval
M1……...primary motor cortex (or sensorimotor cortex)
MFG……....middle frontal gyrus
MNI…….Montreal Neurological Institute
MRT……median reaction time
NMDA……N-methyl D-asparate
N1……first negative-going ERP component
N2……second negative-going ERP component
OCD……obsessive-compulsive disorder
OFC……orbital frontal cortex
PCP……..phencyclidine
PET……..positron emission tomography
PD……Parkinson's Disease
PI…….probability of inhibition (also P(i))
PFC……..prefrontal cortex
PMC…….premotor cortex
PR…….probability of responding (also P(r))

P3…….third positive going ERP component
preSMA……...pre-supplementary motor area (or anterior supplementary motor area)
ROI……..region of interest
RTs……..reaction times
SANS……...scale for the assessment of negative symptoms
SAPS……....scale for the assessment of positive symptoms
SFG……..superior frontal gyrus
SMA……supplementary motor area
SNr……..substantia nigra *pars reticulate*
SOA……stimulus onset asynchrony
SSD…….stop-signal delay
SSRT……...stop-signal reaction time
STN…….subthalamic nucleus
STG…….superior temporal gyrus
STR…….striatum
SVC…….small volume correction
Thal…….thalamus
TMS……transcranial magnetic stimulation
VLFPC……ventrolateral prefrontal cortex
VTA……ventral tegmental area
WCST……Wisconsin card sorting test
ZRFT……...z relative finishing time

Abstract

The capacity to inhibit planned or on-going action enables individuals to flexibly control behaviour in response to changing task demands or a change in goals. This capacity, termed *response inhibition*, is a core function of the executive control system and is often studied in laboratory settings using the stop-signal paradigm, which was used for studying response inhibition throughout this thesis. The stop-signal paradigm (Logan & Cowan, 1984) is increasingly being used by research groups to study response inhibition largely due to the indices of behavioural control afforded by stop-signal procedures, notably the speed of response inhibition processes and the capacity to trigger these processes.

Lesion, transcranial magnetic stimulation and neuroimaging experiments have linked stopping to activity in the right inferior frontal gyrus (IFG), and some evidence indicates a role for the subthalamic nucleus (STN). These brain areas are thought to form a network which acts by suppressing thalamo-cortical output to motor cortex. Event-related potential studies have linked stopping to amplitude enhancement of an N1-P3 complex during successful inhibition trials compared to unsuccessful inhibition trials.

The primary aim of this thesis was to investigate the spatio-temporal dynamics of stop-signal inhibition in healthy individuals using electrophysiological and neuroimaging methods, and secondly, to investigate the neural basis of impaired stopping in patients with a diagnosis of schizophrenia – the first of its kind using the stop-signal paradigm. Several previous behavioural studies have reported slowed stop-signal response inhibition processes in patients with schizophrenia, but an impaired capacity to trigger response inhibition processes has also been reported.

In each of the three neuroimaging studies detailed herein, stopping was related to activation in right IFG and STN, and in one study a model for the difficulty of inhibition was proposed, which predicted activity in this network. Consistent with previous reports, stopping processes in patients with schizophrenia were slower compared to controls, and right IFG and STN were uniquely underactivated in the patient group. Additionally, one study revealed a link between response inhibition speed and both Stop-P3 amplitude, and the latency difference between N1 and P3 potential peaks elicited on stop-signal trials.