



Universiteit  
Leiden  
The Netherlands

## **The role of the locus coeruleus-noradrenaline system in temporal attention and uncertainty processing**

Brown, S.B.R.E.

### **Citation**

Brown, S. B. R. E. (2015, June 16). *The role of the locus coeruleus-noradrenaline system in temporal attention and uncertainty processing*. Retrieved from <https://hdl.handle.net/1887/33220>

Version: Corrected Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/33220>

**Note:** To cite this publication please use the final published version (if applicable).

Cover Page



Universiteit Leiden



The handle <http://hdl.handle.net/1887/33220> holds various files of this Leiden University dissertation

**Author:** Brown, Stephen B.R.E.

**Title:** The role of the locus coeruleus-noradrenaline system in temporal attention and uncertainty processing

**Issue Date:** 2015-06-16

**The role of the locus coeruleus-noradrenaline system in  
temporal attention and uncertainty processing**

**Stephen B.R.E. Brown**

**The work presented in this dissertation was funded by the Netherlands  
Organisation for Scientific Research.**

**ISBN: 978-94-6299-053-1**

**Printing: Ridderprint B.V., Ridderkerk**

**Cover: Ridderprint B.V., Ridderkerk.**

**Copyright © 2015 by Stephen B.R.E. Brown**

**The role of the locus coeruleus-noradrenaline system in temporal attention  
and uncertainty processing**

**Proefschrift**

**ter verkrijging van  
de graad van Doctor aan de Universiteit Leiden,  
op gezag van Rector Magnificus  
prof.mr. C.J.J.M. Stolker,  
volgens besluit van het College voor Promoties  
te verdedigen op  
dinsdag 16 juni 2015  
klokke 16.15 uur.**

**door**

**Stephen B.R.E. Brown  
geboren te Tilburg  
in 1985**

*Leden van de promotiecommissie*

Prof.dr. J.L. Kenemans (Universiteit Utrecht)  
Prof.dr. K.R. Ridderinkhof (Universiteit van Amsterdam)  
Dr. G.P.H. Band

*Promotores*

Prof.dr. S.T. Nieuwenhuis  
Prof.dr. B. Hommel

## Contents

1. General introduction .....	11
<b>1.1 Introduction</b> .....	<b>12</b>
<b>1.2 The locus coeruleus: neuroanatomy</b> .....	<b>12</b>
<b>1.3 The LC-NE system</b> .....	<b>14</b>
<b>1.4 The influence of NE on cognition</b> .....	<b>14</b>
<b>1.4.1. A gain-based account of NE functioning</b> .....	<b>15</b>
<b>1.4.2. A learning account of NE functioning</b> .....	<b>17</b>
<b>1.4.3. A network reset account of NE functioning</b> .....	<b>19</b>
<b>1.5 Acetylcholine</b> .....	<b>19</b>
<b>1.6 An overview of this dissertation</b> .....	<b>21</b>
<i>1.6.1. NE and temporal attention</i> .....	21
<i>1.6.1.1. Functional significance of the emotion-related late positive potential</i> .....	22
<i>1.6.1.2. The effect of clonidine and scopolamine on temporal attention as measured in the attentional blink paradigm</i> .....	23
<i>1.6.1.3. The effect of clonidine and scopolamine on temporal attention as measured in the accessory stimulus paradigm</i> .....	25
<i>1.6.2. NE and learning</i> .....	27
<i>1.6.2.1. The effect of clonidine and scopolamine on learning as reflected by the P3 ERP</i> .....	28
<i>1.6.2.2. The relationship between NE, arousal, pupil diameter, and Hebbian learning</i> .....	31
2. Functional significance of the emotion-related late positive potential .....	33
<b>2.1 Introduction</b> .....	<b>34</b>
<b>2.2 Experiment 1</b> .....	<b>37</b>
<b>2.3 Materials and Methods</b> .....	<b>39</b>
<b>2.3.1. Participants</b> .....	<b>39</b>
<b>2.3.2. Task</b> .....	<b>39</b>
<b>2.3.3. EEG recording and analyses</b> .....	<b>42</b>
<b>2.4 Results</b> .....	<b>43</b>
<i>2.4.1. Late positive potential</i> .....	43
<i>2.4.2. Behavioral results</i> .....	43

2.4.3. <i>LPP-behavior correlations</i> .....	44
2.4.4. <i>Within-subject comparisons between LPP amplitude quartiles</i> .....	44
<b>2.5 Discussion</b> .....	<b>45</b>
<b>2.6 Experiment 2</b> .....	<b>47</b>
<b>2.7 Materials and Methods</b> .....	<b>48</b>
2.7.1. <i>Participants</i> .....	48
2.7.2. <i>Task</i> .....	48
2.7.3. <i>EEG recording and analyses</i> .....	49
<b>2.8 Results</b> .....	<b>50</b>
2.8.1. <i>Late positive potential (LPP)</i> .....	50
2.8.2. <i>P1/N1 complex</i> .....	50
2.8.3. <i>LPP-P1/N1 correlations</i> .....	52
2.8.4. <i>Within-subject comparisons between LPP amplitude quartiles</i> .....	53
2.8.5. <i>Behavioral results</i> .....	55
<b>2.9 Discussion</b> .....	<b>55</b>
<b>2.10 General Discussion</b> .....	<b>56</b>
3. <i>Effects of clonidine and scopolamine on multiple target detection in rapid serial visual presentation</i> .....	61
<b>3.1 Introduction</b> .....	<b>62</b>
<b>3.2 Methods and Materials</b> .....	<b>65</b>
3.2.1. <i>Participants</i> .....	65
3.2.2. <i>Task</i> .....	66
3.2.3. <i>Procedure</i> .....	66
3.2.4. <i>EEG recording and analyses</i> .....	68
<b>3.3 Results</b> .....	<b>69</b>
3.3.1. <i>Physiological and alertness data</i> .....	69
3.3.2. <i>Behavioral data</i> .....	70
3.3.3. <i>Electrophysiological data</i> .....	73
<b>3.4 Discussion</b> .....	<b>75</b>
4. <i>Noradrenergic and cholinergic effects on speed and sensitivity measures of phasic alerting</i> .....	80
<b>4.1 Introduction</b> .....	<b>81</b>



<b>4.2 Methods.....</b>	<b>84</b>
4.2.1. <i>Participants</i> .....	84
4.2.2. <i>Task</i> .....	85
4.2.3. <i>Procedure</i> .....	86
4.2.4. <i>Analyses</i> .....	87
<b>4.3 Results.....</b>	<b>88</b>
4.3.1. <i>Physiological and alertness data</i> .....	88
<b>4.3.2. Effect of AS on reaction times and perceptual sensitivity .....</b>	<b>88</b>
4.3.3. <i>Effect of treatment on AS effect</i> .....	90
<b>4.4 Discussion .....</b>	<b>90</b>
4.4.1. <i>Accessory stimuli enhance perceptual sensitivity</i> .....	90
4.4.2. <i>The AS effect is not mediated by a phasic noradrenergic response</i> .....	94
5. Noradrenergic and cholinergic modulation of late ERP responses to deviant stimuli .....	99
<b>5.1 Introduction.....</b>	<b>100</b>
<b>5.2 Methods.....</b>	<b>102</b>
5.2.1. <i>Participants</i> .....	102
5.2.2. <i>Task</i> .....	103
5.2.3. <i>Procedure</i> .....	104
5.2.4. <i>EEG recording and analyses</i> .....	105
<b>5.3 Results.....</b>	<b>106</b>
5.3.1. <i>Physiological and alertness data</i> .....	106
5.3.2. <i>Behavioral Results</i> .....	108
5.3.3. <i>Standard ERP analyses</i> .....	109
5.3.4. <i>Spatiotemporal principal components analysis</i> .....	111
<b>5.4 Discussion .....</b>	<b>118</b>
6. Effects of arousal on cognitive control: Empirical tests of the conflict-modulated Hebbian-learning hypothesis .....	129
<b>6.1 Introduction.....</b>	<b>130</b>
<b>6.2 Experiment 1 .....</b>	<b>134</b>
<b>6.3 Methods.....</b>	<b>136</b>
6.3.1. <i>Participants</i> .....	136

6.3.2. Stimuli and Task.....	136
6.3.3. Design and Procedure.....	137
6.3.4. Pupil data acquisition and analysis .....	138
<b>6.4 Results.....</b>	<b>138</b>
6.4.1. Behavior .....	138
6.4.2. Pupillometry.....	140
6.4.3. Behavior-pupil correlations .....	142
<b>6.5 Discussion .....</b>	<b>143</b>
<b>6.6 Experiment 2 .....</b>	<b>146</b>
<b>6.7 Methods.....</b>	<b>147</b>
6.7.1. Participants .....	147
6.7.2. Stimuli and Task.....	147
<b>6.8 Results.....</b>	<b>148</b>
6.8.1. Manipulation check.....	149
6.8.2. AS effect on learning rate .....	149
<b>6.9 Discussion .....</b>	<b>151</b>
<b>6.10 General Discussion.....</b>	<b>151</b>
7. General discussion and future directions .....	155
<b>7.1 Introduction.....</b>	<b>156</b>
<b>7.2 The role of the LC-NE system in temporal attention.....</b>	<b>156</b>
<b>7.3 The role of the LC-NE system in learning .....</b>	<b>157</b>
<b>7.4 On the possible interactions between the noradrenergic and cholinergic neuromodulator systems.....</b>	<b>159</b>
<b>7.5 Future directions.....</b>	<b>160</b>
<b>7.6 Concluding remarks .....</b>	<b>162</b>
8. Nederlandse samenvatting .....	165
<b>8.1 De locus coeruleus en noradrenaline .....</b>	<b>166</b>
<b>8.2 De invloed van NE op cognitie .....</b>	<b>166</b>
<b>8.3 De rol van noradrenaline in temporele aandacht.....</b>	<b>169</b>
8.3.1. Hoofdstuk 2: Functionele significantie van de late positive potential (LPP) .....	169

8.3.2. Hoofdstuk 3: <i>De effecten van clonidine en scopolamine op temporele aandacht zoals gemeten met de attentional blink-taak</i> .....	170
8.3.3. Hoofdstuk 4: <i>De effecten van clonidine en scopolamine op het accessory stimulus-effect</i> .....	171
<b>8.4 De rol van noradrenaline in leren.....</b>	<b>172</b>
8.4.1. Hoofdstuk 5: <i>Het effect van clonidine en scopolamine op leren, zoals gereflecteerd door de P3-ERP</i> .....	173
8.4.2. Hoofdstuk 6: <i>De relatie tussen noradrenaline, arousal, pupildiameter, en Hebbiaans leren</i> .....	174
9. References .....	177
Acknowledgements .....	201
Curriculum Vitae .....	203

Tears and fears and feeling proud  
to say, "I love you," right out loud.  
Dreams and schemes and circus crowds:  
I've looked at life that way.

Oh, but now, old friends, they're acting strange  
and they shake their heads  
and they tell me that I've changed.  
Well, something's lost and something's gained  
in living every day.

I've looked at life from both sides now:  
from win and lose,  
and still somehow,  
it's life's illusions I recall.

I really don't know life at all.

- Joni Mitchell, *Both Sides Now*