する眼球運動との相互関係の研究は少なく[5)6)]，未だ不明な点も多い．

人は対象になるものを明確に見るためには，網膜上の中心窩に像を結ばせる必要があり，そのために眼球を動かさなければならない．すなわち眼球運動が生じる．その動きを詳細に検討づけていくことにより，どのように外界に関わろうとしているかを明らかにしていくことができると考えられる[2)3)]．共同研究者らは，視覚刺激として，「泣き」と「怒り」表情の呈示図や赤ん坊の「泣き」の表情写真を用いた際の，陽性・陰性感情のイメージ想起が精神生理学的指標である探索眼球運動に及ぼす影響を検討した．その結果，眼球運動の総移動距離が，陽性感情イメージ想起時では延長し，陰性感情イメージ想起時では短縮することを報告した[4)5)]．そこで本研究では，イメージ想起と呈示する表情写真をマッチングさせ，同時に「笑い声」または「泣き声」の音声を負荷した．また，探索眼球運動をより顕著に促すために，同一の赤ん坊の写真を左右対称に2つ呈示した．さらに，再陽性感情負荷による探索眼球運動の回復過程を詳細に検討するために条件5として陽性感情を再々負荷した．そして，これらの感情状態が精神生理学的指標である探索眼球運動に及ぼす影響を検討したので報告する．

また，検査施行および臨床応用するにあたり，検査結果の再現性の検討は重要な問題であるため，本研究では，1カ月をおき再現性も検討した．

対象および方法

1．対 象

健常ペイドボランティア（79名：平均±標準偏差：36.3±10.9歳，18～60歳）（男性：42名：36.6±10.2歳，女性：37名：36.0±11.6歳）であった．また，本検査の再現性を検討するため，これらの被験者の内20名（34.0±9.4歳，24～54歳，男性：12名，女性：8名）に対し，1カ月後に再度同じ手続きで検査を行った．総ての被験者は，過去に精神的疾病や薬物依存等の既往は無く，麻痺等の神経学的問題も無かった．総ての被験者には，当研究を書面にて説明し同意を得た．なお，当研究は，久留米大学倫理委員会の承認を得ている．

2．探索的眼球運動計測システム

眼球運動検査には，アイマーク・レコーダー（ナック社：EMR-8）を使用した．アイマーク・レコーダーの原理は，眼の角膜に光源からの光（850nm）を当て，その反射光をカメラで捉えるというものである．そして，眼球が動くと，反射光もそれに対応して動くので，これと被験者が見ている背景を写した別のカメラからの映像を重ね合わせることによって，被験者がどこを見ているのかをそのまま観察することができる仕組みになっている．また，記録はアイマーク・レコーダーを通してビデオテープに録画した．

暗い静かな部屋で被験者を椅子に座らせ，できるだけ不安を取り除いた上で，アイマーク・レコーダーを装着した．呈示図（赤ん坊の「笑い」または「泣き」の表情写真）のスライドは，プロジェクターによって，スクリーンの両脇のスピーカーから音声（赤ん坊の笑い声・泣き声：70dB）とともに200cm前方の150×100cmのスクリーンに映写した．なお，注視停留点は，視角1°以上で停留時間100msec以上とし，10秒間の動きをデータとし解析した．また，瞬きの影響を考慮して，本研究では，500cm/sec以上の眼球の動きおよびスクリーン外の注視点は削除した．

3．解析要素

a．平均移動距離　総移動距離を停留点総数で割ったものである．これは視野の広がりを示す指標であると考えられる．単位はcmである．

b．総移動距離　それぞれの注視点間の距離を測定して，個々の移動距離を求め，それをすべて加えたものである．これは10秒間の視覚的な行動の遂行における総合的なエネルギーを示す指標であると考えられる．単位はcmである．

c．平均停留時間　それぞれの注視点が一カ所にどのくらいの時間停留したかをひとつひとつ測定し，その平均を算出したものである．これは注意の平均的な分配時間を示す指標であると考えられる．単位は秒である．

d．停留点総数　注視停留点の数をすべて加えたものである．これは注意の分散の度合いを示す指標であると考えられる．単位は個とした．

4．検査方法

はじめに，全ての被験者に対し，{今から見せる写真について，後でどんな写真を見たか尋ねますので，よく注意して見てください}と指示した．これは，遅延課題となり探索を促す．

条件1：｛楽しいことを思い出してください｝と指示し，｛思い出しました｝との返事の後，｛思っていてください｝と指示し，楽しい事をイメージ想起した状況で，赤ん坊の「笑い」写真を「笑い声」とともに15秒間呈示した．

条件2：｛悲しいことを思い出してください｝と指示し，｛思い出しました｝との返事の後，｛思っていてください｝と指示し，悲しい事をイメージ想起した状況で，赤ん坊の「泣き」写真を「泣き声」とともに15秒間呈示した．

条件3：｛最も悲しいことを思い出してください｝と指示し，｛思い出しました｝との返事の後，｛思っていてください｝と指示し，最も悲しい事をイメージ想起した状況で，赤ん坊の「泣き」写真を「泣き声」とともに15秒間呈示した．

条件4：1分間の休息後，再び｛楽しいことを思い出してください｝と指示し，｛思い出しました｝との返事の後，｛思っていてください｝と指示し，楽しい事をイメージ想起した状況で，赤ん坊の「笑い」写真を「笑い声」とともに15秒間呈示した．

条件5：1分間の休息後，再び｛楽しいことを思い出してください｝と指示し，｛思い出しました｝との返事の後，｛思っていてください｝と指示し，楽しい事をイメージ想起した状況で，赤ん坊の「笑い」写真を「笑い声」とともに15秒間呈示した．

5．統計処理

探索眼球運動解析要素（平均移動距離，総移動距離，平均停留時間，停留点総数）に関して検定を行った．まず，被験者に対する指示が異なる条件を主効果にして一元配置の分散分析を行った．次に多重比較検定を Fisher の PLSD（protected least significant difference）で行った．相関は，ピアソンの積率相関を用い，Bartlett の検定を使用した．なお，危険率5％未満をもって有意とした．

結　　果

1．注視停留点の動き

注視停留点は，陽性感情を惹起させた条件では，笑った赤ん坊の，最も情報に富む領域（両目や口元等）を含み広く大きく動いた．その反面，陰性感情を惹起させた条件では，泣いている赤ん坊の左右の写真の中央付近に注視停留点は集まり，動きも不活発であった．また，右目も左目も同様の動きを示した（図1参照）．

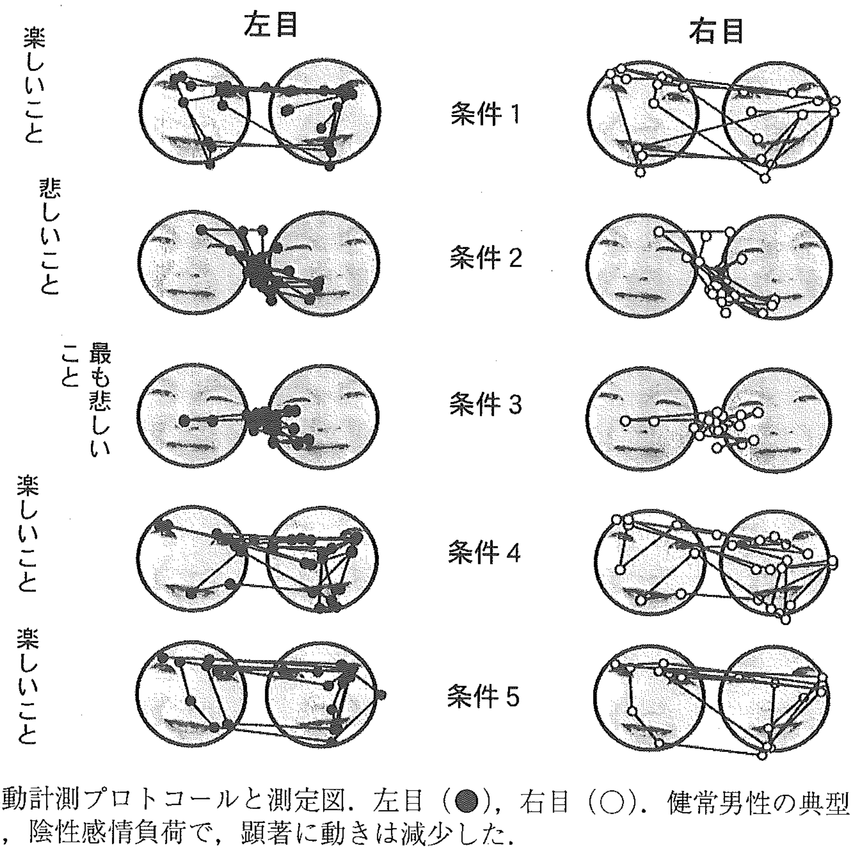


図1　眼球運動計測プロトコールと測定図．左目（●），右目（○）．健常男性の典型例．図でわかる様に，陰性感情負荷で，顕著に動きは減少した．

2．解析要素

a．平均移動距離

注視点の平均移動距離において，条件の主効果が認められ [$F(4,762)=18.1$, $p<0.0001$]，多重比較の結果，条件1と条件2（$p<0.0001$），条件3（$p<0.0001$）および条件2と条件4（$p<0.0001$），条件5（$p<0.001$）（図2では省略）および条件3と条件4（$p<0.0001$），条件5（$p<0.0001$）の間で有意な差が認められた．なお，条件2と条件3および条件4と条件5の間に有意差は認められなかった．

b．総移動距離

注視点の総移動距離において，条件の主効果が認められた [$F(4,762)=37.6$, $p<0.0001$]．多重比較の結果，条件1と条件2（$p<0.0001$），条件3（$p<0.0001$），条件4（$p<0.05$）および条件2と条件4（$p<0.0001$），条件5（$p<0.0001$）（図2では省略）および条件3と条件4（$p<0.0001$），条件5（$p<0.0001$）の間に有意な差が認められた．なお，条件2と条件3および条件4と条件5の間に有意差は認められなかった．

c．平均停留時間

注視点の平均停留時間において，条件の主効果が認められ [$F(4,762)=22.5$, $p<0.0001$]，多重比較の結果，条件1と条件2（$p<0.0001$），条件3（$p<0.0001$）および条件2と条件4（$p<0.0001$），条件5（$p<0.0001$）（図3では省略），条件3と条件4（$p<0.0001$），条件5（$p<0.0001$）

表1　各条件における，総移動距離，平均移動距離，平均停留時間，停留点総数の平均値および標準偏差．

	笑い1	泣き2	泣き3	笑い4	笑い5
総移動距離（cm）	455.7±153.8	309.6±140.8	284.9±129.2	412.9±170.7	434.5±176.5
平均移動距離（cm）	19.03±5.42	15.52±5.57	14.86±5.61	18.66±6.04	19.08±6.53
平均停留時間（秒）	0.248±0.08	0.312±0.113	0.332±0.132	0.268±0.090	0.245±0.059
停留点総数（個）	26.15±5.83	22.37±6.29	21.23±6.05	24.58±5.92	25.74±5.56

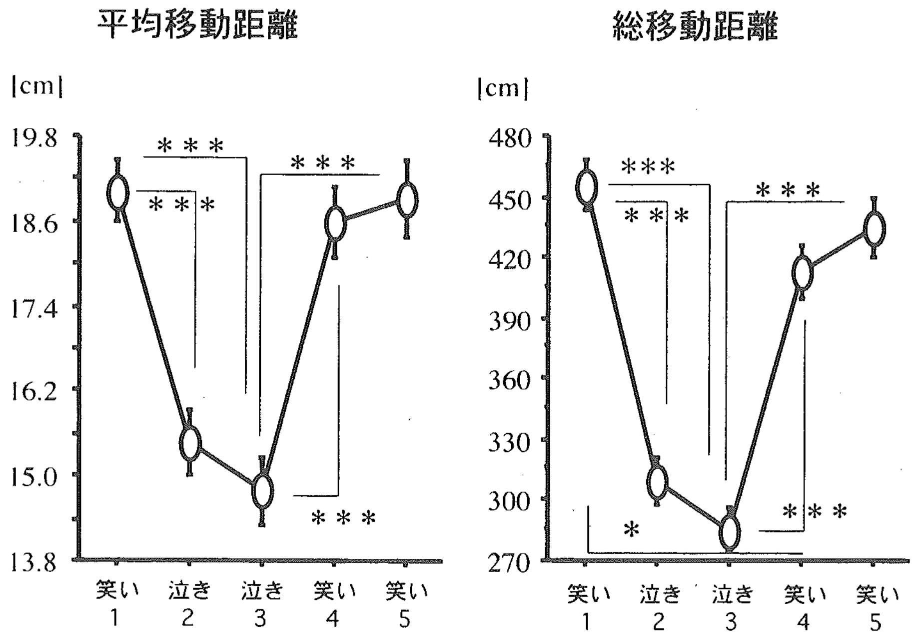


図2　平均移動距離（左）と総移動距離（右）．縦軸に解析要素を横軸に条件をとりグラフを作成した．移動距離は，陰性感情負荷で有意に短縮した．
*：$p<0.05$，**：$p<0.01$，***：$p<0.001$．

および条件4と条件5（$p<0.05$）の間で有意な差が認められた．なお，条件2と条件3および条件4と条件5の間に有意差は認められなかった．

d．停留点総数

注視点の停留点総数において，条件の主効果が認められ［$F(4,762)=18.2$，$p<0.0001$］，多重比較の結果，条件1と条件2（$p<0.0001$），条件3（$p<0.0001$），条件4（$p<0.05$）および条件2と条件4（$p<0.001$），条件5（$p<0.0001$）（図3では省略）および条件3と条件4（$p<0.001$），条件5（$p<0.0001$）の間で有意な差が認められた．なお，条件2と条件3および条件4と条件5の間に有意差は認められなかった．

3．眼球運動の再現性の検討

a．平均移動距離において，試行1と試行2とは有意は正の相関（$r=0.710$，$p<0.0001$）が観察された．また，各条件においても試行1と試行2とは有意な正の相関（条件1：$r=0.609$，$p<0.01$，条件2：$r=0.664$，$p<0.01$，条件3：$r=0.604$，$p<0.01$，条件4：$r=0.592$，$p<0.01$，条件5：$r=0.834$，$p<0.0001$）が観察された．なお，試行1と試行2の間に有意差は認められなかった．

b．総移動距離において，試行1と試行2とは有意は正の相関（$r=0.764$，$p<0.0001$）が観察された．また，各条件においても試行1と試行2とは有意な正の相関（条件1：$r=0.657$，$p<0.01$，条件2：$r=0.695$，$p<0.01$，条件3：$r=0.772$，$p<0.001$，条件4：$r=0.687$，$p<0.01$，条件5：$r=0.829$，$p<0.0001$）が観察された．なお，試行1と試行2の間に有意差は認められなかった（図4参照）．

c．平均停留時間において，試行1と試行2とは有意な正の相関（$r=0.531$，$p<0.0001$）が観察された．また，各条件においても試行1と試行2とは有意な正の相関（条件1：$r=0.686$，$p<0.001$，条件3：$r=0.603$，$p<0.01$，条件5：$r=0.564$，$p<0.05$）が観察された．なお，試行1と試行2の間に有意差は認められなかった．

d．停留点総数において，試行1と試行2とは有意な正の相関（$r=0.551$，$p<0.0001$）が観察された．また，各条件においても試行1と試行2とは有意な正の相関（条件1：$r=0.506$，$p<0.05$，条件3：$r=0.603$，$p<0.01$，条件5：$r=0.564$，$p<0.05$）が観察された．なお，試行1と試行2の間に有意差は認められなかった．

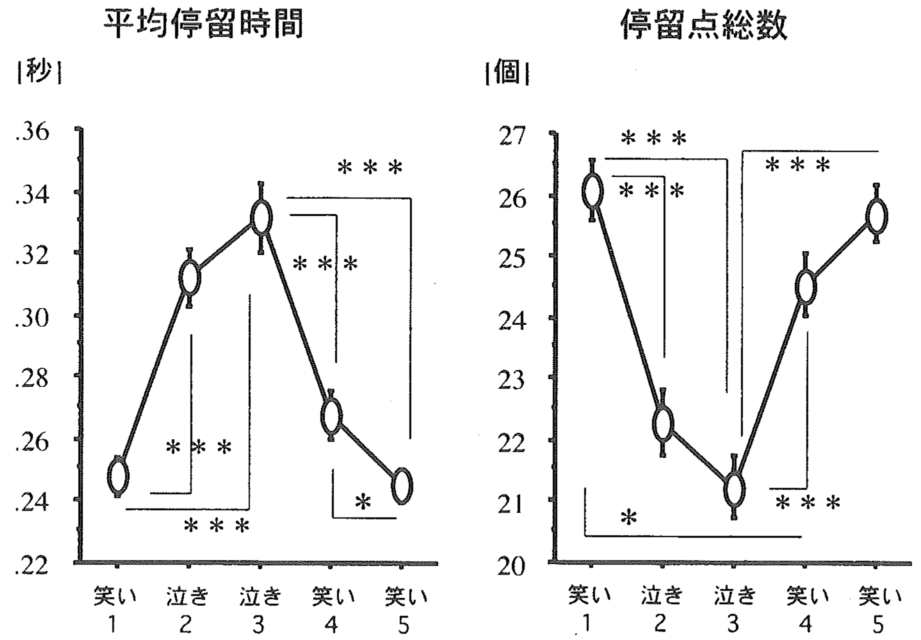


図3　平均停留時間（左）と停留点総数（右）．縦軸に解析要素を横軸に条件をとりグラフを作成した．陰性感情負荷で，平均停留時間は有意に延長し，停留点総数は有意に減少した．
＊：$p<0.05$，＊＊＊：$p<0.001$．

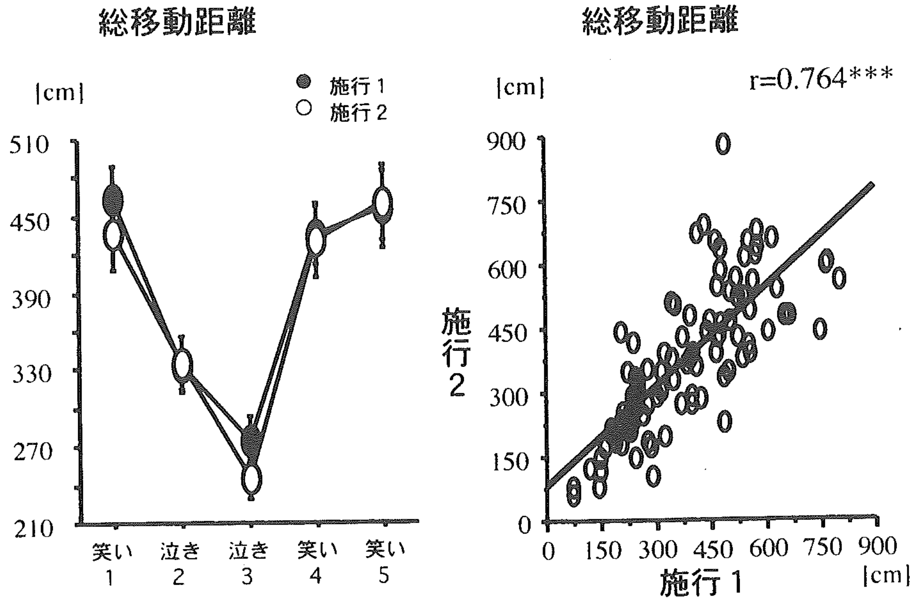


図4　探索眼球運動の再現性．施行1と施行2の総移動距離（左）とその相関関係（右）．
＊：$p<0.05$，＊＊＊：$p<0.001$．

考　　察

人が対象なるものを明確に見るためには，網膜上の中心窩に像を結ばせる必要があり，注視点の動き，すなわち眼球運動が生じる．その動きを詳細に調べていくことにより，人がどのように対象物を認知しようとしているのかを明らかにできると考えられる[2)3)]．{後からどんな写真を見たか尋ねますので，よく注意して見てください}と教示することによって，被験者の探索行動を促し，その時の注視点の動きを計測し，検討していくことは人の視覚的認知機能および心理状態を客観的に捉える上で，大変有用であると考えられる[3)−7)]．

これまでの研究において，上野ら[4)]は，健常者を対象に陽性（楽しい）・陰性（悲しい）感情をイメージ想起させ，簡単な表情提示画「泣き」または「怒り」を見せた際の探索眼球運動を検討した．その結果，「泣き」「怒り」条件とも，注視停留点の総移動距離は，陰性感情イメージ想起時では短縮し，再陽性感情イメージ想起時では延長した．また，森田ら[5)]は，健常者を対象に陽性（楽しい）・陰性（悲しい）感情をイメージ想起させ，一人の赤ん坊の「泣き」の写真を呈示した際の探索眼球運動を検討した．その結果，イメージ想起した感情と表情写真はミスマッチしているにもかかわらず，注視停留点の総移動距離は，陰性感情イメージ想起時では抑制され，再陽性感情イメージ想起時では促進された．

そこで，本研究では，より陽性（楽しい）・陰性（悲しい）感情を惹起させるために，イメージ想起と呈示する表情写真をマッチングさせ，同時に「笑い声」と「泣き声」の音声を負荷した．また，探索眼球運動をより顕著に促すために，同じ赤ん坊の写真を左右対称に2つ呈示した．さらに，再陽性感情負荷による探索眼球運動の回復過程を検討するために条件5として陽性感情を再々負荷した．その結果，先行研究同様，探索眼球運動は，陰性感情イメージ想起時では抑制され，再陽性感情イメージ想起時では促進された．

情動反応とは，一般的に，感情状態の変化に伴い，急激な生理的変化と行動の変調を伴う著しい反応とされる．情動反応には，表情，発声，姿勢などの外的な表出行動と心拍や瞳孔などの自律神経反応がある[8)−11)]．一般的に，恐怖により「目が点になる」「目が泳ぐ」などの言葉にも見られるように，人の眼の動きは感情状態の変化に伴う表出行動として経験的にとらえられてきた．しかし，これまで眼球運動の変化と情動の関係についての報告は少ない[4)5)]．本研究では，（悲しい）イ

メージ想起と「泣き」の音声を加えた表情写真の呈示により，探索眼球運動は有意な抑制変化を示し，（楽しい）という再イメージ想起と音声を負荷した「笑い」の表情写真の呈示により陰性感情負荷前の状態に回復する現象が観察された．これらの眼球運動の変化は，（楽しい）（悲しい）という感情状態に伴う人の情動反応としてとらえることができると考えられる．つまり，探索眼球運動は陽性・陰性情動を反映する精神・心理生理学的指標になり得ると考えられる．

富田[12]は，うつ病患者を対象に，横「S」字を用いた探索眼球運動の研究において，うつ病患者は，健常者に比べて，注視点数が少なくなることを報告し，この注視点数の減少が外界への関心の減退やそれに基づく行動の減少と相関があることを明らかにしている．本研究では，注視点の総数において，陽性感情負荷条件と陰性感情負荷条件の間に有意な差が観察され，陽性感情負荷条件では増加し，陰性感情負荷条件では減少するという結果を示した．人の眼球運動には，視野の中で認知すべき対象の方向に視線を向けるための探索的運動と視野の中にある対象物を認知する運動がある．また，人が対象物を認知する過程における心理的要因について友久[13]は，無数にある刺激の中から特定の対象物を「認知する」ということは，個体が何かの特定の物を見ようとする積極的な準備状態にあって初めて可能であり，ここに知覚するという働きが成立すると述べ，さらにこの準備状態こそ「基本的態度」であり，「心的構え」であって，一見，生理的と見なされる視認知が，心理的な態度と密接に関連していると述べている．このように眼球運動が観察者の視野内にある，特徴を持った対象物に対して生じ，また視覚刺激を認知するに際し，積極的な準備状態が要求されるとすれば，眼球運動には，観察者の外界への関心の持ち方と対象物に対する働きかけが重要な要素となる．つまり，陰性感情状態において，眼球運動が減少するのは，呈示された表情写真に対し，関わりを持とうとする積極的準備状態である「心的構え」が低下したことによると考えられる．また，これらの眼球運動の乏しさは，余剰性の乏しさと表現することができるように思われる[14]．すなわち，（最も悲しい）という強い陰性感情を伴った過去の記憶をイメージ想起することにより，情動の覚醒レベルが過覚醒状態に陥り，内面的なゆとりがなくなったため，その結果，能動性や外界に対する関心が低下したと考えられる．

回復過程については，総移動距離および停留点総数において，条件1（笑い1：コントロール）と条件4（笑い4：回復過程その1）の間で有意な差が認められ，一方，平均移動距離および平均停留時間においては，条件1と条件4の間に有意差は観察されなかった．また，条件1と条件5の間には，全ての解析要素において，有意な差は観察されなかった．これらの結果から，視野の広がりおよび注意の平均的な分配時間は，再陽性感情を負荷することによって，より短時間で陰性感情負荷前の状態まで回復するが，探索行動の遂行に要する総合的なエネルギーおよび注意の分散の度合いは短時間では戻らず，さらに再々陽性感情を惹起することによって，よりコントロール状態に回復することが観察された．先行研究では，再び陽性感情（楽しいこと）をイメージ想起すると，総移動距離は本研究の条件4と同様にすぐにコントロール状態に回復するという結果が報告されているが，本研究では，再び陽性感情（楽しいこと）をイメージ想起したにもかかわらず，完全にコントロール状態までは回復しなかった．これは，表情写真のマッチングと音声による感情負荷によって，より強い陰性情動状態が惹起され，持続した可能性も否定できない[4]．他の要因としては，呈示写真の違いや解析時間の違いの検討も必要であろう．今後，今回用いた呈示写真と同様の写真をミスマッチさせた条件の検討も必要であろう[5]．

また，すべての解析要素において，（悲しいこと）・（最も悲しいこと）という異なる場面をイメージ想起したにも関わらず，条件2（悲しいこと）と条件3（最も悲しいこと）の間には有意な差が認められなかった．このことから，イメージ想起する内容は異なっても，（悲しい）という陰性感情状態では，探索眼球運動は同程度に抑制されると考えられる．「眼は心の窓」と言われるように些細な情動に敏感に反応すると考えられる．他の可能性として，コントロール状態で眼球運動が大きい被験者では，条件2と条件3に有意差が観察された（未発表）ことより，計測時における「構え」に関連する可能性も考えられる[3]．

最後に，検査施行および臨床応用するにあたり，

検査結果の再現性は重要な問題であるため，本研究では，20名の被験者に対し，1カ月の期間をおき，再度同様の手続きで検査を行った．その結果，今回用いた全ての解析要素において，施行間に有意差は観察されなかった．また，施行間に有意な正の相関が観察された．以上の結果から，本検査の再現性は十分あると考えられる．前田9)が精神疾患における情動機構の重要性を提唱しているように，今後，刻一刻と病態が変化していく患者様の視覚的認知機能，特に情動機能を理解する尺度として，本研究は臨床的な応用が可能であると考えられる．

文　献

1）Holzman PS, Kringle E, Levy DL, Proctor LR, Haberman SJ, Yashillo NJ：Abnormal pursuit eye movement in schizophrenia. Evidence for genetic indicator. Arch Gen Psychiatry, **34**：802 - 805, 1977

2）松島英介，太田克也：認知の生理学的評価．精神医学レビュー No. 27 精神疾患の認知障害（丹羽真一編），第1版，東京，ライフ・サイエンス，85 - 96, 1998

3）Kojima T, Matsushima E, Nakajima K, Shiraishi H, Ando K：Eye movements in acute, chronic and remitted schizophrenics. Biol Psychiatry, **27**：975 - 989, 1990

4）上野雄文，森田喜一郎，早稲田芳史，平井聡，前田久雄：精神分裂病者の探索眼球運動における情動の影響 ―健常者との比較検討―．臨床神経生理学，**30**：60 - 66, 2002

5）森田喜一郎，富田　克，上野雄文，平井　聡，山本寛子，前田久雄：精神分裂病者と健常者の眼球運動 ―赤ちゃんの表情の影響―．臨床脳波，**44**：154 - 159, 2002

6）Miyahira A, Morita K, Yamaguchi H, Nonaka K, Maeda H：Gender differences of exploratory eye movements: Life span study Life Science, **68**：569 - 577, 2000

7）Ryu H, Morita K, Shoji Y, Waseda Y, Maeda H：Abnomal exploratory eye movements in shizophrenic patients vs healthy subjects. Acta Neuro: Scand, **104**：369 - 376, 2001

8）鈴木直人：情動の心理学．感情心理学への招待 ―感情・情緒へのアプローチ（濱　治世，鈴木直人，濱保久著），第1版，東京，サイエンス社，107 - 136, 2001

9）前田久夫：精神疾患における情動の意義．臨床精神薬理，**3**：823 - 830, 2000

10）川村光毅，小幡邦彦：情動の機構と歴史的考察．脳の科学，**20**：709 - 716, 1998

11）松本　元：脳の構成論的研究からみた情動．脳と精神の医学，**6**：365 - 382, 1995

12）富田　堯：うつ病患者の眼球運動．眼とこころ ―眼球運動による精神疾患へのアプローチ（島薗安雄監修），第1版，東京，創造出版，177 - 185, 1991

13）友久久雄：ゲシュタルト認知と心的態度との関連．黒丸正四郎教授満15周年記念論文集．神戸大学医学部精神神経科学教室，113 - 122, 1975

14）小島卓也：精神疾患における認知障害の重要性 ―精神分裂病を中心に．精神医学レビュー No. 27 精神疾患の認知障害（丹羽真一編），第1版，東京，ライフ・サイエンス，5 - 15, 1998

（受付 平成17年4月26日）

久留米医学会雑誌　第68巻　第5・6号　平成17年6月

THE EFFECT OF POSITIVE AND NEGATIVE EMOTION ON THE EXPLORATORY EYE MOVEMENTS

Yohei Ishii[1], Kiichiro Morita[2], Sachiko Nishiura[3],
Hisayoshi Okamura[1], Kiyoshi Makita[2]
Kouji Kurakake[2] and Akira Tsuda[4]

[1]*Graduate School of Psychology, Kurume University*
[2]*Cognitive and molecular of Brain disease, Kurume University*
[3]*Department of Psychiatry, Kurume University School of Medicine*
[4]*Department of Psychology, Kurume University*

The object of the present study was to examine the effect of positive and negative emotion on the exploratory eye movements in healthy subjects.

Methods. Subjects included 79 healthy volunteers (42 men and 37 women) ranging in age from 18 to 60 years. Exploratory eye movements were recorded using an eye-mark recorder. Before recording, all subjects were asked, "Watch baby's photograph carefully. After examination, I asked what kind of photograph did you see?" to examine exploratory eye movements.

Condition 1 (C1) : All subjects were asked, "Recall and image pleasurable event". After all subjects responded, "Yes, imaging" and asked, "Imaging continuously" and presented a smiling baby's photograph with smiling sound.

Condition 2 (C2) : All subjects were asked, "Recall and image sad events". After all subjects responded, "Yes, imaging" and asked, "Imaging continuously" and presented a crying baby's photograph with crying sound.

Condition 3 (C3) : All subjects were asked, "Recall and image the most sad event". After all subjects responded, "Yes, imaging" and asked, "Imaging continuously" and presented a crying baby's photograph with crying sound.

Condition 4 (C4) : After 1 minute rest, exploratory eye movements were recorded with the procedure as the same as C1.

Condition 5 (C5) : After 1 minute rest, Exploratory eye movements were recorded again with the procedure as the same as C1.

Results. The mean eye scanning length (MESL) and the total eye scanning length (TESL) were clearly reduced during recalling and imaging sad events and recovered significantly after recalling and imaging pleasurable events.

The mean eye fixation time (MEFT) was extended during recalling and imaging sad events and recovered significantly after recalling and imaging pleasurable events.

The total number of eye fixations points (TNEFP) was clearly decreased during recalling and imaging sad events and recovered significantly after recalling and imaging pleasurable events.

In addition, to examine the reproduction of this study, the same inspection was done one month later. As a result, the difference was not observed between the initial results and the following results in four measures (MESL, TESL, TNEFP, MEFT). Also, the positive correlation was observed between the initial results and the following results.

Conclusions. Exploratory eye movements may be a useful biological index to evaluate positive and negative emotions.

ELSEVIER

NeuroImage

www.elsevier.com/locate/ynimg
NeuroImage 23 (2004) 967–974

Brain activation associated with evaluative processes of guilt and embarrassment: an fMRI study

Hidehiko Takahashi,[a,b] Noriaki Yahata,[c] Michihiko Koeda,[d] Tetsuya Matsuda,[e] Kunihiko Asai,[b] and Yoshiro Okubo[c,*]

[a]*Section of Psychiatry and Behavioral Science, Graduate School of Medicine, Tokyo Medical and Dental University, Japan*
[b]*Asai Hospital, Japan*
[c]*Department of Neuropsychiatry, Nippon Medical School, Japan*
[d]*Department of Bioinformatics, Medical Research Institute, Tokyo Medical and Dental University, Japan*
[e]*Brain Activity Imaging Center, Tamagawa University Research Institute, Japan*

Received 21 January 2004; revised 5 June 2004; accepted 19 July 2004
Available online 6 October 2004

We aimed to investigate the neural substrates associated with evaluative process of moral emotions. Using functional magnetic resonance imaging (fMRI), we examined the similarities and differences between evaluative process of guilt and that of embarrassment at the neural basis level. Study of the neural basis of judgments of moral emotions might contribute to a better understanding of the amoral behavior observed in neurological and psychiatric disorders. Nineteen healthy volunteers were studied. The participants read sentences carrying neutral, guilty, or embarrassing contents during the scans. Both guilt and embarrassment conditions commonly activated the medial prefrontal cortex (MPFC), left posterior superior temporal sulcus (STS), and visual cortex. Compared to guilt condition, embarrassment condition produced greater activation in the right temporal cortex (anterior), bilateral hippocampus, and visual cortex. Most of these regions have been implicated in the neural substrate of social cognition or Theory of Mind (ToM). Our results support the idea that both are self-conscious emotions, which are social emotions requiring the ability to represent the mental states of others. At the same time, our functional fMRI data are in favor of the notion that evaluative process of embarrassment might be a more complex process than that of guilt.

Keywords: Guilt; Embarrassment; Social cognition; Theory of Mind; Medial prefrontal cortex; Superior temporal sulcus

Introduction

Although there have been numerous neuroimaging studies on primary emotions (fear, disgust, happiness, and sadness) that have led to a better understanding of the neuroanatomical correlates of emotions (Phan et al., 2002), only a few studies on complex social emotions such as guilt, shame, and embarrassment have been reported. These social emotions have been viewed as moral emotions because they occur in response to moral violation and promote moral behavior, interpersonal etiquette, and personal hygiene (Eisenberg, 2000; Haidt, 2003). At the same time, these emotions inhibit transgression of social standards and motivate reparative action such as apology, confession, and atonement.

Impairment of possessing the mental states of these moral emotions could lead to amoral, inappropriate behaviors observed in neurological and psychiatric disorders such as brain injuries (Anderson et al., 1999; Beer et al., 2003), frontotemporal dementia (Miller et al., 2003; Snowden et al., 2002), autism (Capps et al., 1992; Frith, 2001; Hillier and Allinson, 2002), and antisocial personality (Brower and Price, 2001; Moll et al., 2003). Studying the neural substrates of judgments of moral emotions should add to the understanding of the neural basis of amoral behaviors observed in neurological and psychiatric disorders.

From a psychological point of view, guilt, shame, embarrassment, and pride are categorized into the same emotion family, "self-conscious emotions". "Self-conscious emotions" are emotions founded in social relationship and arise from concerns about others' opinions of self or the behavior of self (Eisenberg, 2000; Haidt, 2003; Tangney and Dearing, 2002). Negative evaluation of self or the behavior of self is fundamental to guilt, shame, and embarrassment, while positive evaluation of self leads to pride. In other words, one needs the ability to represent the mental states of others (intention/emotion), that is, Theory of Mind (ToM), to recognize self-conscious emotions. The recognition of negative self-conscious emotions involves understanding of the violation of social norms and the negative evaluation of self, both important aspects of ToM. Children with autism demonstrating impaired ToM showed impaired recognition of self-conscious emotions (Heerey et al., 2003). In line with this notion, a recent functional magnetic resonance imaging (fMRI) study demonstrated activation in the medial prefrontal cortex (MPFC), temporal regions, and orbito-

---

* Corresponding author. Department of Neuropsychiatry, Nippon Medical School, 1-1-5, Sendagi, Bunkyo-ku, Tokyo, 113-8603 Japan. Fax: +81 3 5814 6280.
E-mail address: okubo-y@nms.ac.jp (Y. Okubo).

1053-8119/$ - see front matter © 2004 Elsevier Inc. All rights reserved.
doi:10.1016/j.neuroimage.2004.07.054

frontal cortex (OFC) during the emotional judgments of embarrassment (Berthoz et al., 2002). These areas have been implicated in ToM, social cognition, and moral judgment (Adolphs, 2001; Allison et al., 2000; Frith, 2001; Frith and Frith, 1999; Greene and Haidt, 2002; Greene et al., 2001; Moll et al., 2003; Pinkham et al., 2003). However, a previous positron emission tomography (PET) study using a guilt-related script reported a slightly different activation pattern in anterior paralimbic regions during the experience of guilt (Shin et al., 2000). In the former fMRI study, an emotional judgment task was used. Participants read various kinds of stories depicting embarrassing situations and were instructed to imagine what the story protagonist (participant himself or a third person in the story) would feel. In the latter PET study, an emotion induction method was used. Participants listened to audio-taped personal events involving the most guilt they had actually experienced. They recalled and imagined the event as if they were actually participating in it again. These two studies differed in the emotional tasks and measurement methods, making it difficult to compare the results directly. To our knowledge, no neuroimaging study has as yet investigated the different types of self-conscious emotions and compared the neural activation patterns directly in one session.

Although the distinctions among guilt, shame, and embarrassment are not clear-cut, psychologists have challenged this issue. Although embarrassment has traditionally been considered to be a variant of shame (Lewis, 1993), recent psychological data support the notion that embarrassment is an emotion distinct from other self-conscious emotions (Keltner and Buswell, 1997). Embarrassment has higher affinity to violation of social conventions, while guilt and shame have higher affinity to violation of a moral norm (Eisenberg, 2000; Haidt, 2003; Tangney et al., 1996). In this sense, among the negative self-conscious emotions, distinction between guilt and embarrassment is considered to be relatively clear-cut. Therefore, we focused on these two emotions.

We used block-design fMRI to measure regional activation associated with judgments of guilt and embarrassment during an emotional judgment task presenting short sentences. Emotion processing is composed of evaluative, experiential, and expressive components. We did not intend to induce emotional states because we thought it would be difficult to induce emotional states of guilt or embarrassment by merely having the subjects read short sentences. Moreover, it would be difficult to control the situation so as not to induce emotions other than guilt and embarrassment (e.g., anger, shame, sadness) as reported in the previous induction study (Shin et al., 2000). We aimed to elucidate the similarities and differences between the evaluative process of guilt and that of embarrassment at the neural basis level by measuring neural activation during judgments of both emotions in a session using fMRI.

We hypothesized that both emotional conditions would commonly activate the components of the neural substrates (MPFC, superior temporal sulcus (STS)) that have been implicated in social cognition (Adolphs, 2001; Allison et al., 2000) or ToM (Frith, 2001; Frith and Frith, 1999), and at the same time, would show differences in the extent of activation of the components.

Method

Participants

Nineteen healthy right-handed Japanese subjects (10 men, mean age 30.8 years, SD = 6.2; nine women, mean age 25.1 years, SD = 3.2) were recruited from the surrounding community. Their mean educational achievement level was 16.2 years (SD = 2.1). They did not meet criteria for any psychiatric disorder. None of the controls were taking alcohol or medication at the time, nor did they have a history of psychiatric disorder, significant physical illness, head injury, neurological disorder, or alcohol or drug dependence. All subjects underwent an MRI to rule out cerebral anatomic abnormalities. After complete explanation of the study, written informed consent was obtained from all subjects, and the study was approved by the Ethics Committee.

Materials

Because our experimental design was a block design, we aimed to control readability, the number of words, and luminance across blocks using short sentences. In addition, we expected participants to make emotional judgments repeatedly in a block. For this reason, we used short sentences instead of other forms, for example, stories. Three types of short sentences were provided (neutral, guilt, and embarrassment). Each sentence was written in Japanese and in the first person, past tense. Each sentence was expected to carry guilt, embarrassment, or no prominent emotional content. To validate our expected results, other healthy volunteers (10 men and 10 women, mean age 28.6 years, SD = 3.7) than the subjects participating in this fMRI study were screened. They read each sentence and rated the described situations according to how guilty or embarrassing they seemed using a 6-point analog scale (1 = none, 6 = extremely intense). As we predicted, the mean ratings of guilt and embarrassment for neutral sentences were 1.0 (SD = 0.1) and 1.0 (SD = 0.1), for guilt-related sentences 4.4 (SD = 0.4) and 1.6 (SD = 0.4), and for embarrassing sentences 1.5 (SD = 0.3) and 3.5 (SD = 0.5), respectively. Examples of the sentences are shown in Table 1. The sentences were projected via a computer and a telephoto lens onto a screen mounted on a head coil. The subjects were instructed to read the sentences silently and were told that they would rate the described situations according to how guilty or embarrassing they seemed. After reading each sentence, the subjects were instructed to press a selection button with the right index finger, indicating that they had read and understood it. The experimental design consisted of six blocks for each of the three conditions (neutral, guilt, and embarrassment) interleaved with 20-s rest periods. The order of presentation for the three conditions was fixed in the neutral–guilt–embarrassment sequence (Fig. 1). During the rest condition,

Table 1
Examples of sentences

Neutral	I used a cellular phone in the park. I used a computer on the internet. I change into pajamas at night. I washed my clothes. I had dinner at the restaurant.
Guilt	I used a cellular phone in the hospital. I sent a computer virus by e-mail. I shoplifted a dress from the store. I betrayed my friend. I left the restaurant without paying.
Embarrassment	I was not dressed properly for the occasion. I mistook a stranger for my friend. I noticed that the zipper of my pants was open. I soiled my underwear. I did not know the right behavior at the restaurant.

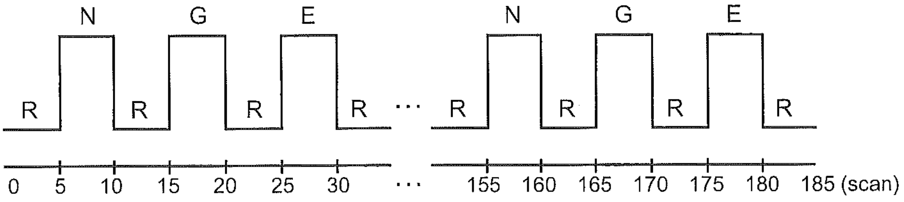


Fig. 1. Block design paradigm in the fMRI study. R = rest, N = neutral, G = guilt, E = embarrassment.

participants viewed a crosshair pattern projected to the center of the screen. In each 20-s block, five different sentences of the same emotional class were presented for 4 s each. After the scan, subjects rated the described situations according to how guilty or embarrassing they seemed using a 6-point analog scale.

Image acquisition

Images were acquired with a 1.5-T Signa system (General Electric, Milwaukee, WI). Functional images of 185 volumes were acquired with T2*-weighted gradient echo planar imaging sequences sensitive to the blood oxygenation level dependent (BOLD) contrast. Each volume consisted of 40 transaxial contiguous slices with a slice thickness of 3 mm to cover almost the whole brain (flip angle, 90°; TE, 50 ms; TR, 4 s; matrix, 64 × 64; field of view, 24 × 24 cm). High-resolution, T1-weighted anatomic images were acquired for anatomic comparison (124 contiguous axial slices, 3D Spoiled-Grass sequence (SPGR), slice thickness 1.5 mm, TE, 9 ms; TR, 22 ms; flip angle, 30°; matrix, 256 × 192; field of view, 25 × 25 cm).

Analysis of functional imaging data

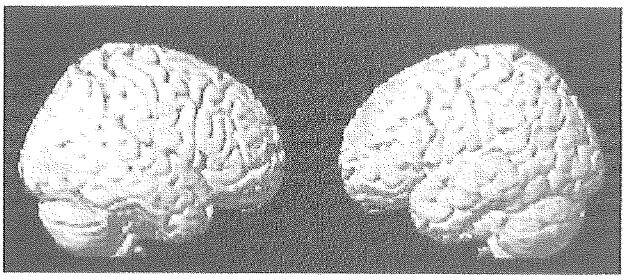
Data analysis was performed with statistical parametric mapping software package (SPM99) (Wellcome Department of Cognitive Neurology, London, UK) running with MATLAB (Mathworks, Natick, MA). All volumes were realigned to the first volume of each session to correct for subject motion and were spatially normalized to the standard space defined by the Montreal Neurological Institute (MNI) template. After normalization, all scans had a resolution of 2 × 2 × 2 mm^3. Functional images were spatially smoothed with a 3D isotropic Gaussian kernel (full width at half maximum of 8 mm). Low frequency noise was removed by applying a high-pass filter (cutoff period = 240 s) to the fMRI time series at each voxel. A temporal smoothing function was applied to the fMRI time series to enhance the temporal signal-to-noise ratio. Significant hemodynamic changes for each condition were examined using the general linear model with boxcar functions convoluted with a hemodynamic response function. Statistical parametric maps for each contrast of the t statistic were calculated on a voxel-by-voxel basis. The t values were then transformed to unit normal distribution, resulting in Z scores.

To assess the specific condition effect, we used the contrasts of guilt minus neutral (G − N) and embarrassment minus neutral (E − N). A random effects model, which estimates the error variance for each condition across subjects, was implemented for group analysis. This procedure provides a better generalization for the population from which data are obtained. The contrast images were obtained from single-subject analysis and were entered into the group analysis. A one-sample t test was applied to determine group activation for each effect. Significant clusters of activation were determined using the conjoint expected probability distribution of the height and extent of Z scores with the height ($Z > 3.09$; $P <$

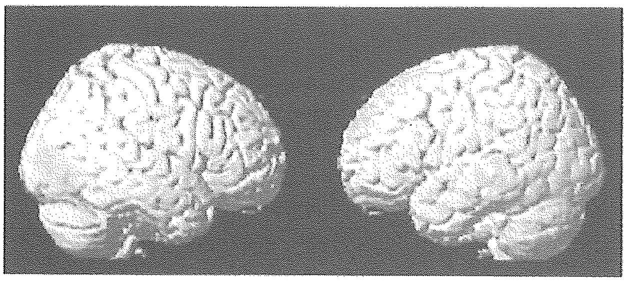
Table 2
Brain activation in guilt condition and embarrassment condition relative to neutral condition

Brain region	Coordinates			BA	*Z* score	Voxels
	x	*y*	*z*			
Guilt minus neutral						
L visual cortex (cuneus, LG)	−6	−95	12	17,18,19	4.55	1114
R visual cortex (LG)	2	−85	6	17,18	5.41	
L MPFC (MFG, SFG)	−16	49	9	6,8,9,10	4.7	1175
R MPFC (MFG)	4	57	16	9,10	3.62	
L posterior STS (MTG)	−44	−61	20	39	4.4	210
Embarrassment minus neutral						
L visual cortex (cuneus, LG, FG)	−2	−89	4	17,18,19	4.91	4343
R visual cortex (cuneus, LG)	20	−70	0	17,18	5.52	
L MPFC (MFG, SFG)	−8	50	25	6,8,9,10	4.44	840
R MPFC (MFG, SFG)	2	59	17	9,10	3.75	
L posterior STS (MTG, STG)	−42	−59	18	39	4.24	185
L middle temporal cortex (MTG)	−51	−31	−7	21	4.56	132
L anterior temporal cortex (MTG)	−53	1	−24	21	4.3	50
R anterior temporal cortex (MTG, FG)	48	−7	−27	20	3.69	44
L OFC (IFG)	−44	31	−7	47	3.68	36
L hippocampus	−34	−18	−18		3.85	23

Coordinates and Z score refer to the peak of each brain region. BA = Brodmann area; L = left; R = right; LG = lingual gyrus; FG = fusiform gyrus; MFG = medial frontal gyrus; SFG = superior frontal gyrus; MTG = middle temporal gyrus; STG = superior temporal gyrus; IFG = inferior frontal gyrus; MPFC = medial prefrontal cortex; STS = superior temporal sulcus; OFC = orbitofrontal cortex.



Guilt minus neutral



Embarrassment minus neutral

Fig. 2. Images showing brain activation in guilt and embarrassment conditions relative to neutral condition. Guilt minus neutral (top). Activated regions were in the MPFC, posterior STS, and visual cortex. Embarrassment minus neutral (bottom). In addition to activations in the MPFC, left posterior STS, and visual cortex, more widespread activations were shown in the left OFC, left temporal cortex (anterior and middle), and right temporal cortex (anterior). Note that both emotional conditions commonly activated the MPFC, left posterior STS, and visual cortex. Significant differences were recognized at a height threshold ($Z > 3.09$; $P < 0.001$, uncorrected) and extent threshold (15 voxels).

0.001, uncorrected) and extent threshold (15 voxels). We used a relatively large extent threshold to sufficiently minimize the risk of type 1 errors due to the relatively low height threshold. To assess common areas activated by the guilt and embarrassment conditions, we created a mask from the G − N contrast in the random effect analysis (threshold at $P < 0.001$, uncorrected). This mask was applied inclusively to the E − N contrast.

To ensure relative differences between activity associated with guilt and embarrassment, random effect analyses of guilt minus embarrassment contrast (G − E) and embarrassment minus guilt contrast (E − G) were conducted. Because one of the aims of this study was to investigate differences between guilt and embarrassment at the neural basis level, we reported the differences at a lower threshold (height threshold at $P < 0.005$, uncorrected, and extent threshold of 15 voxels).

We conducted additional analysis to demonstrate a more direct link between regional brain activity with subjective emotional judgments. Using the mean of ratings of guilt and embarrassment for each subject as the covariate, regression analyses with the contrast (G − N and E − N) and the covariate were done at the second level (height threshold at $P < 0.001$, uncorrected, and extent threshold of 15 voxels). Using the effect sizes, representing the percent signal change, of the contrasts (E − N and G − N) at the peak coordinates uncovered by regression analyses, we plotted fMRI signal changes and ratings of guilt and embarrassment. Coordinates of activation were converted from MNI coordinates to the Talairach and Tournoux (1988) coordinates using the mni2tal algorithm (M. Brett, Cambridge, MA).

Results

Self-rating

The neutral sentences were judged as carrying neither guilty nor embarrassing contents. The mean ratings of guilt and embarrassment for neutral sentences were, respectively, 1.0 (SD = 0.0) and 1.0 (SD = 0.0), for guilt-related sentences 4.1 (SD = 0.7) and 1.6 (SD = 0.7), and for embarrassing sentences 1.5 (SD = 0.4) and 3.7 (SD = 0.6). The mean ratings of guilt were significantly greater for guilt-related sentences than for embarrassing sentences ($t = 10.6$, $df = 36$, $P < 0.001$). The mean ratings of embarrassment were significantly greater for embarrassing sentences than for guilt-related sentences ($t = 12.4$, $df = 36$, $P < 0.001$).

fMRI result

Guilt condition relative to neutral condition (G − N) produced greater activations in the MPFC, left posterior STS, and visual cortex. Embarrassment condition relative to neutral condition (E − N) produced greater activations in the MPFC, left posterior STS, left temporal cortex (anterior and middle), left orbitofrontal cortex (OFC), right temporal cortex (anterior), left hippocampus, and visual cortex (Table 2 and Fig. 2). In other words, both conditions commonly activated the MPFC, left posterior STS, and visual cortex (Table 3), but the embarrassment condition produced more widespread activations in the left temporal cortex (anterior and middle), right temporal cortex (anterior), left OFC, and left hippocampus.

Embarrassment condition relative to guilt condition (E − G) produced greater activation in the right temporal cortex (anterior), bilateral hippocampus, and visual cortex. In contrast, guilt condition relative to embarrassment condition (G − E) produced greater activation in the MPFC (Table 4 and Fig. 3).

Regression analyses revealed positive linear correlations between self-rating of guilt and the degree of activation in the

Table 3

Brain regions commonly activated by guilt and embarrassment conditions

Brain region	Coordinates			BA	*Z* score	Voxels
	x	*y*	*z*			
L visual cortex (LG)	−12	−77	6	17,18,19	4.37	1021
R visual cortex (LG)	2	−85	6	17,18	5.41	
L MPFC (MFG, SFG)	−10	36	52	8,9,10	4.35	429
R MPFC (MFG)	4	57	16	10	3.62	
L posterior STS (MTG)	−44	−61	20	39	4.4	101

A mask from the G − N contrast by random effect analysis (threshold at $P < 0.001$, uncorrected) was applied inclusively to the E − N contrast (height threshold at $P < 0.001$, uncorrected, and extent threshold of 15 voxels). See Table 2 legend.

Table 4
Comparisons between regional brain activities associated with guilt and embarrassment

Brain region	Coordinates			BA	Z score	Voxels
	x	y	z			
Embarrassment minus guilt						
R visual cortex (cuneus, LG, FG)	12	−83	8	17,18,19	3.28	393
R visual cortex (IOG)	38	−68	−5	19	3.59	49
L visual cortex (LG)	−10	−62	−2	18,19	3.48	140
L visual cortex (LG)	−8	−80	1	19	2.86	77
R anterior temporal cortex (MTG)	42	−3	−27	21	2.96	25
R hippocampus	32	−18	−13		2.91	32
L hippocampus	−20	−14	−9		3.21	49
Guilt minus embarrassment						
L MPFC (MFG)	−16	49	14	10	3.39	24

Random effect analyses of G − E and E − G contrast were conducted. See Table 2 legend.

MPFC (medial frontal gyrus, $x = -8, y = 55, z = 3$; $Z = 4.26$; 31 voxels), posterior STS (middle temporal gyrus, $x = -58$, $y = -56$, $z = 10$; $Z = 4.23$; 81 voxels), and visual cortex (lingual gyrus, $x = -14$, $y = -58$, $z = 3$; $Z = 3.82$; 24 voxels). There were positive linear correlations between self-rating of embarrassment and the degree of activation in the posterior STS (middle temporal gyrus, $x = -46$, $y = -57$, $z = 23$; $Z = 3.88$; 37 voxels) and visual cortex (lingual gyrus, $x = -16$, $y = -49$, $z = -4$; $Z = 3.48$; 20 voxels) (Figs. 4 and 5).

Discussion

We investigated the neural response associated with evaluative processes of self-conscious moral emotions. Recent neuroimaging studies have reported the neural substrate of moral judgment (Greene et al., 2001; Moll et al., 2002a,b). However, few reports are available on specific moral or social emotions (Berthoz et al., 2002; Shin et al., 2000). This study showed similarities and differences during evaluative processes of two moral emotions, guilt and embarrassment, at the neural basis level by measurements of neural responses in the same session.

As we predicted, both guilt and embarrassment conditions relative to neutral condition commonly produced greater activity in the components of neural substrates of social cognition or ToM, the MPFC, left posterior STS, along with the visual cortex. Several neuroimaging studies in healthy subjects using different variants of the ToM paradigm have consistently reported activation in the MPFC, predominantly on the left side (Fletcher et al., 1995; Gallagher et al., 2000; Goel et al., 1995). Additionally, autism, which is considered to have impairments in ToM, showed reduced activation in the MPFC (Baron-Cohen et al., 1999; Castelli et al., 2002; Happe et al., 1996). The MPFC has been suggested to play an important role in monitoring one's own mental state as well as that of others (Castelli et al., 2000; Frith, 2001). Recent studies reported that the MPFC was also recruited in moral judgment (Greene et al., 2001; Heekeren et al., 2003).

Activations in the posterior STS have also been consistently reported in social cognition or ToM tasks (Calder et al., 2002; Castelli et al., 2000; Gallagher et al., 2000; Winston et al., 2002) and in moral judgment tasks (Greene et al., 2001; Heekeren et al., 2003), while the area identical to the posterior STS was variously described as the temporoparietal junction or angular gyrus. Originally, STS was known to be activated by biological motions such as movement of eyes, mouth, hands, and body, but it has been suggested to have a more general function in social cognition (Adolphs, 2001; Allison et al., 2000), detection of intention (Gallagher et al., 2000), evaluation of trustworthiness of faces (Winston et al., 2002), detection of the behavior of agents and analysis of goal, and outcome of the behavior (Frith, 2001; Frith and Frith, 1999).

Common activations in the MPFC and posterior STS support the notion that both guilt and embarrassment are self-conscious

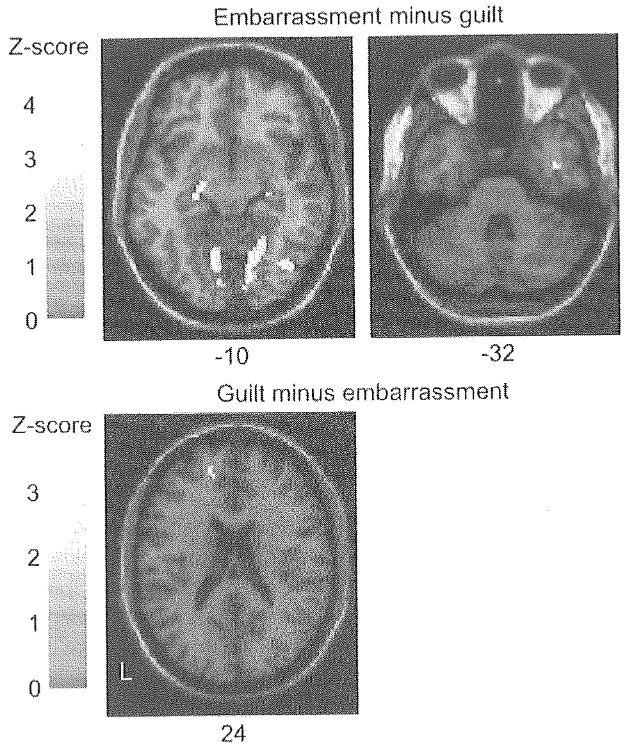


Fig. 3. Comparison of guilt and embarrassment conditions with height threshold ($P < 0.005$) and extent threshold (15 voxels). Embarrassment minus guilt (top). Compared to guilt, greater activation was shown in the right temporal cortex (anterior), bilateral hippocampus, and visual cortex. Guilt minus embarrassment (bottom). Compared to embarrassment, greater activation was shown in the MPFC. The bar shows the range of the Z score. Within the image, L indicates left. Numbers in the bottom row indicate the z coordinates of the Montreal Neurological Institute brain.

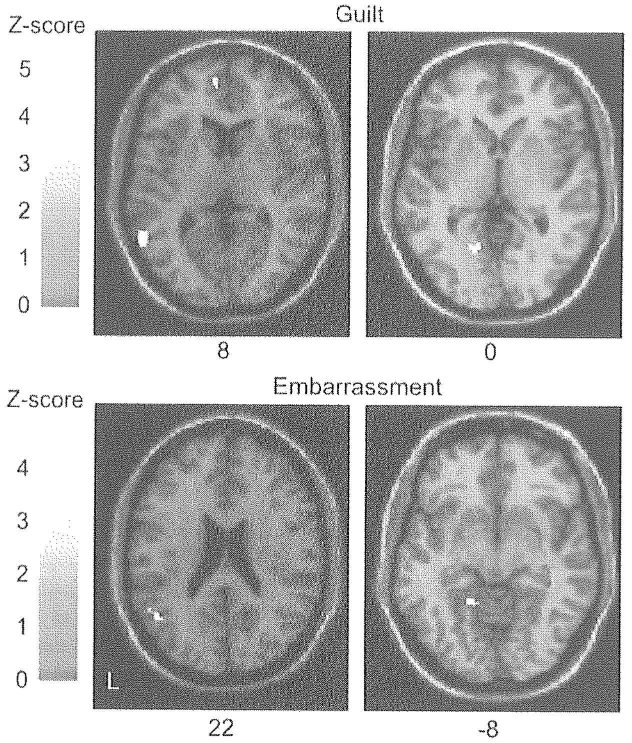


Fig. 4. Correlation between brain activation and the self-ratings of guilt and embarrassment with height threshold ($P < 0.005$) and extent threshold (15 voxels). There were positive linear correlations between self-rating of guilt and the degree of activation in the posterior STS and visual cortex (top). There were positive linear correlations between self-rating of embarrassment and the degree of activation in the posterior STS and visual cortex (bottom). The bar shows the range of the Z score. Within the image, L indicates left. Numbers in the bottom row indicate the z coordinates of the Montreal Neurological Institute brain.

emotions that can arise from concerns about others' evaluation of one's own behavior (Eisenberg, 2000; Haidt, 2003; Tangney and Dearing, 2002). In other words, one needs the ability to take the perspective of others and to represent their mental state, that is, ToM, to understand the sense of guilt or embarrassment.

In spite of our attempt to control the linguistic features of the visual stimuli, increased activations were found in the visual cortex in response to the emotional conditions relative to the neutral condition. Enhanced visual cortex activations by emotionally salient visual stimuli have been extensively reported (Phan et al., 2002; Takahashi et al., 2004). Emotionally salient stimuli or attention demanding stimuli have been suggested as modulating sensory processing in the visual cortex. Early visual cortex receives prominent feedback projection from limbic structures such as amygdala (Emery and Amaral, 2000), and such pathway could act to enhance visual processing (Morris et al., 1998; Vuilleumier et al., 2001).

Interestingly, compared to the G − N contrast, the E − N contrast demonstrated more widespread activations in the left temporal cortex (anterior and middle), right temporal cortex (anterior), left OFC, and left hippocampus. Direct comparison between guilt and embarrassment conditions showed that the E − G contrast demonstrated significantly greater activation in the right anterior temporal cortex, bilateral hippocampus, and visual cortex. All these regions are also considered as the brain area related to social or moral cognition (Adolphs, 2001; Casebeer, 2003; Greene and Haidt, 2002; Moll et al., 2003). We did not expect the greater activation in the hippocampus in the embarrassment condition. The hippocampus is suggested to engage in retrieving behaviorally relevant memories (Strange et al., 1999). In moral judgment, the hippocampus might facilitate conscious recollection of memories that allow past events to affect current decisions (Casebeer, 2003).

Embarrassment has a higher affinity to the violation of social conventions (choices of clothing, etiquette and hygiene, etc.) that depend on societies or cultures, while guilt has a higher affinity to the violation of moral norms (issues of harm, right and justice, etc.) that are universal among human beings (Eisenberg, 2000; Haidt, 2003; Tangney et al., 1996). Moreover, embarrassment is uniquely a public emotion that depends on a real or imagined presence of others among one's self-conscious emotions. If people do experience embarrassment in private, it is a situation of vividly imagining what others might think of them (Miller, 1996; Tangney et al., 1996). Guilt does not necessarily depend on personal acquaintances. Guilt could be elicited not only by concerns with others' evaluation of self but also by private conscience (Haidt, 2003; Tangney and Dearing, 2002; Tangney et al., 1996). In light of these points, embarrassment could be regarded as a more social and public emotion that depends on personal interactions. Regression analyses showed that subjective ratings of guilt and embarrassment correlated with the degree of activation in the posterior STS, visual cortex, and MPFC, brain areas commonly activated by both emotional conditions. In other words, emotional intensity did not appear to account for the more widespread activation observed in embarrassment condition. Considering the regression analyses results, our interpretation was that the additional activations found in embarrassment condition might reflect more complex processes that detect and understand the complex social information of embarrassment.

This study has some limitations. First, a moral emotion could be accompanied by another emotion. For instance, guilt and shame could co-occur in some situations (Eisenberg, 2000). In moral transgression, people may feel guilty for violating a social norm and at the same time might feel shameful about one's own shortcomings. For this reason, we carefully chose the situations, although we understand that it is not feasible to extract "pure" emotion. Second, as mentioned above, embarrassment depends on society and culture. The social background of participants, such as gender, generation, religion, and education, could be confounding factors. Further studies that can control these factors would be recommended. Finally, we should acknowledge general limitations of a functional imaging study to reveal the neural substrates of social cognition or social emotions. The processing of social information is distributed in space and time, ranging from the perception of socially relevant stimuli to the elicitation of social behavior. Most functional imaging studies focused on the perception and interpretation of socially relevant stimuli. Emotional judgment tasks such as facial expression discrimination task or our task could also be regarded as a task of the perception and interpretation of socially relevant stimuli. It should be noted that emotional states that elicit social or emotional behaviors are not necessarily induced by merely viewing facial expressions or reading sentences. Social cognition is a domain with fuzzy boundaries and vaguely specified components. Processes of social cognition overlap with those of emotions. Although it is difficult to assess specific components of social cognition or emotions by a single modality, at least in this study, we assessed the evaluative processes of moral emotions. To complement fMRI studies, electrophysiological methods that have good temporal resolution

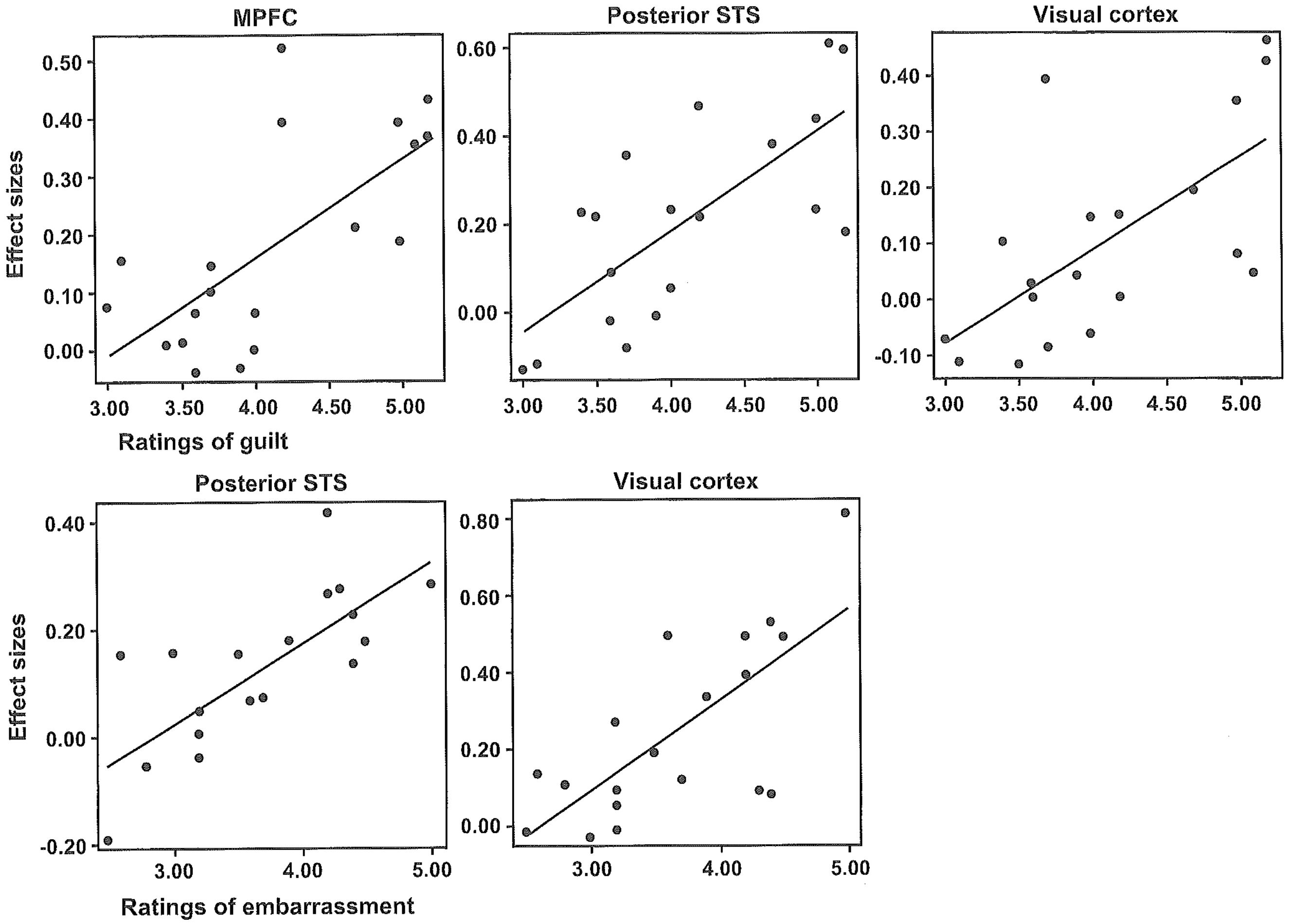


Fig. 5. Plots and regression lines of correlations between self-ratings and degree of activation in the brain regions. There were correlations between self-rating of guilt and degree of activation in the MPFC ($x = -8, y = 55, z = 3, r = 0.686, P < 0.005$), posterior STS ($x = -58, y = -56, z = 10, r = 0.722, P < 0.005$), and visual cortex ($x = -14, y = -58, z = 3, r = 0.653, P < 0.005$) (top). There were positive linear correlations between self-rating of embarrassment and degree of activation in the posterior STS ($x = -46, y = -57, z = 23, r = 0.744, P < 0.005$) and visual cortex ($x = -16, y = -49, z = -4, r = 0.719, P < 0.005$) (bottom).

would be recommended. Moreover, it is difficult to assess real-life human social behavior or to induce complex emotions in an MRI environment. Lesion studies can at least indicate the structures necessary for mediating social behavior (Adolphs, 2003).

Notwithstanding the difficulties in measuring social behavior, recording autonomic responses will be useful for assessing some aspects of social behavior or emotional responses. For instance, monitoring blushing, the hallmark of embarrassment, by recording face temperature or facial blood flow will be useful to distinguish embarrassment from guilt (Gerlach et al., 2003).

In conclusion, we investigated the neural substrates of evaluative processes of specific moral emotions and demonstrated similarities and differences between guilt and embarrassment at the neural basis level. Supporting the concept that both guilt and embarrassment could be regarded as self-conscious emotions, both emotional conditions produced similar activation patterns in the components of neural substrates implicated in social cognition or ToM. Moreover, our fMRI data lead us to conjecture that the evaluative process of embarrassment might be a more complex process than that of guilt. We expect our findings to contribute to a broadening of the knowledge concerning the neural basis of amoral behavior observed in neurological and psychiatric disorders.

Acknowledgments

We thank Professor Toru Nishikawa of the Section of Psychiatry and Behavioral Science, Graduate School of Medicine, Tokyo Medical and Dental University. The staff of the Section of Biofunctional Informatics, Graduate School of Medicine, Tokyo Medical and Dental University, and of Asai Hospital are gratefully acknowledged. This work was supported by a Grant-in-Aid for Scientific Research from the Japanese Ministry of Education, Culture, Sports, Science and Technology (15390348), a research grant for nervous and mental disorders (14B-3), and a Health and Labor Sciences Research Grant for Research on Psychiatric and Neurological Diseases and Mental Health (H15-KOKORO-003) from the Japanese Ministry of Health, Labor and Welfare.

References

Adolphs, R., 2001. The neurobiology of social cognition. Curr. Opin. Neurobiol. 11, 231–239.

Adolphs, R., 2003. Investigating the cognitive neuroscience of social behavior. Neuropsychologia 41, 119–126.

Allison, T., Puce, A., McCarthy, G., 2000. Social perception from visual cues: role of the STS region. Trends Cogn. Sci. 4, 267–278.

Anderson, S.W., Bechara, A., Damasio, H., Tranel, D., Damasio, A.R., 1999. Impairment of social and moral behavior related to early damage in human prefrontal cortex. Nat. Neurosci. 2, 1032–1037.

Baron-Cohen, S., Ring, H.A., Wheelwright, S., Bullmore, E.T., Brammer, M.J., Simmons, A., Williams, S.C., 1999. Social intelligence in the normal and autistic brain: an fMRI study. Eur. J. Neurosci. 11, 1891–1898.

Beer, J.S., Heerey, E.A., Keltner, D., Scabini, D., Knight, R.T., 2003. The regulatory function of self-conscious emotion: insights from patients with orbitofrontal damage. J. Pers. Soc. Psychol. 85, 594–604.

Berthoz, S., Armony, J.L., Blair, R.J., Dolan, R.J., 2002. An fMRI study of intentional and unintentional (embarrassing) violations of social norms. Brain 125, 1696–1708.

Brower, M.C., Price, B.H., 2001. Neuropsychiatry of frontal lobe dysfunction in violent and criminal behaviour: a critical review. J. Neurol., Neurosurg. Psychiatry 71, 720–726.

Calder, A.J., Lawrence, A.D., Keane, J., Scott, S.K., Owen, A.M., Christoffels, I., Young, A.W., 2002. Reading the mind from eye gaze. Neuropsychologia 40, 1129–1138.

Capps, L., Yirmiya, N., Sigman, M., 1992. Understanding of simple and complex emotions in non-retarded children with autism. J. Child Psychol. Psychiatry 33, 1169–1182.

Casebeer, W.D., 2003. Moral cognition and its neural constituents. Nat. Rev., Neurosci. 4, 840–846.

Castelli, F., Happe, F., Frith, U., Frith, C.D., 2000. Movement and mind: a functional imaging study of perception and interpretation of complex intentional movement patterns. NeuroImage 12, 314–325.

Castelli, F., Frith, C.D., Happe, F., Frith, U., 2002. Autism, Asperger syndrome and brain mechanisms for the attribution of mental states to animated shapes. Brain 125, 1839–1849.

Eisenberg, N., 2000. Emotion, regulation, and moral development. Annu. Rev. Psychol. 51, 665–697.

Emery, N.J., Amaral, D.G., 2000. The role of the amygdala in primate social cognition. In: Lane, R.D., Nadel, L. (Eds.), Cognitive Neuroscience of Emotion. Oxford Univ. Press, New York, pp. 156–191.

Fletcher, P.C., Happe, F., Frith, U., Baker, S.C., Dolan, R.J., Frackowiak, R.S., Frith, C.D., 1995. Other minds in the brain: a functional imaging study of "theory of mind" in story comprehension. Cognition 57, 109–128.

Frith, U., 2001. Mind blindness and the brain in autism. Neuron 32, 969–979.

Frith, C.D., Frith, U., 1999. Interacting minds—A biological basis. Science 286, 1692–1695.

Gallagher, H.L., Happe, F., Brunswick, N., Fletcher, P.C., Frith, U., Frith, C.D., 2000. Reading the mind in cartoons and stories: an fMRI study of 'theory of mind' in verbal and nonverbal tasks. Neuropsychologia 38, 11–21.

Gerlach, A.L., Wilhelm, F.H., Roth, W.T., 2003. Embarrassment and social phobia: the role of parasympathetic activation. J. Anxiety Disord. 17, 197–210.

Goel, V., Grafman, J., Sadato, N., Hallett, M., 1995. Modeling other minds. NeuroReport 6, 1741–1746.

Greene, J.D., Haidt, J., 2002. How (and where) does moral judgment work? Trends Cogn. Sci. 6, 517–523.

Greene, J.D., Sommerville, R.B., Nystrom, L.E., Darley, J.M., Cohen, J.D., 2001. An fMRI investigation of emotional engagement in moral judgment. Science 293, 2105–2108.

Haidt, J., 2003. The moral emotions. In: Davidson, R.J., Scherer, K.R., Goldsmith, H.H. (Eds.), Handbook of Affective Sciences. Oxford Univ. Press, Oxford, pp. 852–870.

Happe, F., Ehlers, S., Fletcher, P., Frith, U., Johansson, M., Gillberg, C., Dolan, R., Frackowiak, R., Frith, C., 1996. 'Theory of mind' in the brain. Evidence from a PET scan study of Asperger syndrome. NeuroReport 8, 197–201.

Heekeren, H.R., Wartenburger, I., Schmidt, H., Schwintowski, H.P., Villringer, A., 2003. An fMRI study of simple ethical decision-making. NeuroReport 14, 1215–1219.

Heerey, E.A., Keltner, D., Capps, L.M., 2003. Making sense of self-conscious emotion: linking theory of mind and emotion in children with autism. Emotion 3, 394–400.

Hillier, A., Allinson, L., 2002. Understanding embarrassment among those with autism: breaking down the complex emotion of embarrassment among those with autism. J. Autism Dev. Disord. 32, 583–592.

Keltner, D., Buswell, B.N., 1997. Embarrassment: its distinct form and appeasement functions. Psychol. Bull. 122, 250–270.

Lewis, M., 1993. Self-conscious emotions: embarrassment, pride, shame and guilt. In: Lewis, M., Haviland, J.M. (Eds.), Handbook of Emotions. Guilford Press, New York, pp. 623–636.

Miller, R.S., 1996. Embarrassment: Poise and Peril in Everyday Life. Guilford Press, New York.

Miller, B.L., Diehl, J., Freedman, M., Kertesz, A., Mendez, M., Rascovsky, K., 2003. International approaches to frontotemporal dementia diagnosis: from social cognition to neuropsychology. Ann. Neurol. 54, S7–S10.

Moll, J., de Oliveira-Souza, R., Bramati, I.E., Grafman, J., 2002a. Functional networks in emotional moral and nonmoral social judgments. NeuroImage 16, 696–703.

Moll, J., de Oliveira-Souza, R., Eslinger, P.J., Bramati, I.E., Mourao-Miranda, J., Andreiuolo, P.A., Pessoa, L., 2002b. The neural correlates of moral sensitivity: a functional magnetic resonance imaging investigation of basic and moral emotions. J. Neurosci. 22, 2730–2736.

Moll, J., de Oliveira-Souza, R., Eslinger, P.J., 2003. Morals and the human brain: a working model. NeuroReport 14, 299–305.

Morris, J.S., Friston, K.J., Buchel, C., Frith, C.D., Young, A.W., Calder, A.J., Dolan, R.J., 1998. A neuromodulatory role for the human amygdala in processing emotional facial expressions. Brain 121, 47–57.

Phan, K.L., Wager, T., Taylor, S.F., Liberzon, I., 2002. Functional neuroanatomy of emotion: a meta-analysis of emotion activation studies in PET and fMRI. NeuroImage 16, 331–348.

Pinkham, A.E., Penn, D.L., Perkins, D.O., Lieberman, J., 2003. Implications for the neural basis of social cognition for the study of schizophrenia. Am. J. Psychiatry 160, 815–824.

Shin, L.M., Dougherty, D.D., Orr, S.P., Pitman, R.K., Lasko, M., Macklin, M.L., Alpert, N.M., Fischman, A.J., Rauch, S.L., 2000. Activation of anterior paralimbic structures during guilt-related script-driven imagery. Biol. Psychiatry 48, 43–50.

Snowden, J.S., Neary, D., Mann, D.M., 2002. Frontotemporal dementia. Br. J. Psychiatry 180, 140–143.

Strange, B.A., Fletcher, P.A., Henson, R.N.A., Friston, K.J., Dolan, R.J., 1999. Segregating the functions of human hippocampus. Proc. Natl. Acad. Sci. U. S. A. 96, 4034–4039.

Takahashi, H., Koeda, M., Oda, K., Matsuda, T., Matsushima, E., Matsuura, M., Asai, K., Okubo, Y., 2004. An fMRI study of differential neural response to affective pictures in schizophrenia. NeuroImage 22, 1247–1254.

Talairach, J., Tournoux, P., 1988. Co-Planar Stereotaxic Atlas of the Human Brain: Three-Dimensional Proportional System. Thieme Medical, New York.

Tangney, J.P., Dearing, R.L., 2002. Shame and Guilt. Guilford Press, New York.

Tangney, J.P., Miller, R.S., Flicker, L., Barlow, D.H., 1996. Are shame, guilt, and embarrassment distinct emotions? J. Pers. Soc. Psychol. 70, 1256–1269.

Vuilleumier, P., Armony, J.L., Driver, J., Dolan, R.J., 2001. Effects of attention and emotion on face processing in the human brain: an event-related fMRI study. Neuron 30, 829–841.

Winston, J.S., Strange, B.A., O'Doherty, J., Dolan, R.J., 2002. Automatic and intentional brain responses during evaluation of trustworthiness of faces. Nat. Neurosci. 5, 277–283.

ELSEVIER

NeuroImage

www.elsevier.com/locate/ynimg
NeuroImage 22 (2004) 1247–1254

An fMRI study of differential neural response to affective pictures in schizophrenia

Hidehiko Takahashi,[a,b] Michihiko Koeda,[c] Kenji Oda,[a] Tetsuya Matsuda,[d] Eisuke Matsushima,[d] Masato Matsuura,[e] Kunihiko Asai,[b] and Yoshiro Okubo[f,*]

[a] *Section of Psychiatry and Behavioral Science, Graduate School of Medicine, Tokyo Medical and Dental University, Japan*
[b] *Asai Hospital, Japan*
[c] *Department of Bioinformatics, Medical Research Institute, Tokyo Medical and Dental University, Japan*
[d] *Section of Liaison Psychiatry and Palliative Medicine, Graduate School of Medicine, Tokyo Medical and Dental University, Japan*
[e] *Department of Neuropsychiatry, School of Medicine, Nihon University, Tokyo, Japan*
[f] *Department of Neuropsychiatry, Nippon Medical School, Tokyo 113-8603, Japan*

Received 20 November 2003; revised 24 January 2004; accepted 8 March 2004

Although emotional dysfunction is considered a fundamental symptom of schizophrenia, studies investigating the neural basis of emotional dysfunction in schizophrenia are few. Using functional magnetic resonance imaging (fMRI) and a task viewing affective pictures, we aimed to examine automatic emotional response and to elucidate the neural basis of impaired emotional processing in schizophrenia. Fifteen healthy volunteers and 15 schizophrenics were studied. During the scans, the subjects were instructed to indicate how each of the presented pictures made them feel. Whole brain activities in response to the affective pictures were measured by fMRI. Controls recruited the neural circuit including amygdaloid–hippocampal region, prefrontal cortex, thalamus, basal ganglia, cerebellum, midbrain, and visual cortex while viewing unpleasant pictures. Despite an equal behavioral result to controls, the patients showed less activation in the components of the circuit (right amygdala, bilateral hippocampal region, medial prefrontal cortex (MPFC), basal ganglia, thalamus, cerebellum, midbrain, and visual cortex). This study demonstrated functional abnormalities in the neural circuit of emotional processing in schizophrenia. In particular, decreased activation in the right amygdala and MPFC appears to be an important finding related to dysfunctional emotional behavior in schizophrenia.

Keywords: Schizophrenia; Emotion; Functional magnetic resonance imaging; Amygdala; Prefrontal cortex; Affective pictures

Introduction

Emotional dysfunction such as "flattening affect" or "anhedonia" is considered to be one of the key symptoms of schizophrenia (Andreasen and Flaum, 1991). Recent functional imaging techniques have revealed dysfunction of the neural circuit (interrelationship among cortical region, thalamus, basal ganglia, and cerebellum) in schizophrenia (Andreasen et al., 1999; Schultz and Andreasen, 1999). Most studies focused on cognitive dysfunction (Andreasen et al., 1999), while studies investigating the neural basis of dysfunctional emotional processing in schizophrenia are limited (Gur et al., 2002; Paradiso et al., 2003; Phillips et al., 1999; Schneider et al., 1998; Taylor et al., 2002). Previous neuroimaging studies in normal subjects revealed the neuroanatomical correlates of emotional processing and the crucial role of the amygdala in processing negative emotions. In particular, left-sided activations in the amygdala while processing negative facial expressions have been consistently reported (Calder et al., 2001). Recent functional magnetic resonance imaging (fMRI) studies revealed that schizophrenic patients demonstrated decreased activation in the bilateral amygdala during an emotion induction task by facial expressions (Schneider et al., 1998) or decreased activation in the left amygdala during a discrimination task of emotional facial expressions (Gur et al., 2002). However, discriminating analogous facial expressions is an effortful cognitive process whether subjects categorize the facial expressions by gender or emotion. Cognitive demands for elaborate recognition or detailed rating may modulate the emotional response in the brain (Critchley et al., 2000; Hariri et al., 2000; Keightley et al., 2003; Lange et al., 2003; Taylor et al., 2003). In addition, it should be noted that emotional facial expressions do not necessarily elicit the subjective experience of emotions (Davidson and Irwin, 1999).

Several activation studies used affective pictures to elicit emotion in healthy volunteers (Lane et al., 1997a,b). The task of simply viewing emotionally salient pictures could minimize cognitive demands and would be suitable for examining automatic emotional response. Only a few positron emission tomography (PET) studies have investigated the emotional processing of affective pictures with a task of rating subjective emotional experience (Taylor et al., 2002) or with a task of emotional

---

* Corresponding author. Department of Neuropsychiatry, Nippon Medical School, 1-1-5, Sendagi, Bunkyo, Tokyo 113-8603, Japan. Fax: +81-3-5814-6280.

E-mail address: okubo-y@nms.ac.jp (Y. Okubo).

1053-8119/$ - see front matter © 2004 Elsevier Inc. All rights reserved.
doi:10.1016/j.neuroimage.2004.03.028

perception (Paradiso et al., 2003) in schizophrenia, and these studies have not established consistent results for a better understanding of dysfunctional emotional processing in schizophrenia. To our knowledge, no fMRI study has examined the neural response across the whole brain to affective pictures in schizophrenia. In the present study, we used fMRI and a task with minimal cognitive demands to identify the neural circuit of automatic emotional processing. We expected the subjects to react to affective pictures without an effortful cognitive process and categorize them roughly according to their subjective emotional experiences. Comparing the neural responses of schizophrenic patients with those of healthy controls, we aimed to elucidate the neural basis of impaired emotional processing in schizophrenia.

Methods

Subjects

Fifteen schizophrenic patients (10 men and 5 women, mean age 29.0 years, SD = 6.9) meeting the DSM-IV criteria for schizophrenia were studied. Diagnoses were made by HT, YO, and the psychiatrists in charge based on a review of their charts and a conventionally semi-structured interview. Exclusion criteria were current or past substance abuse and a history of alcohol-related problems, mood disorder, or organic brain disease. Thirteen patients were recruited from the outpatient unit of Asai Hospital, and two were recruited from the inpatient unit. Eleven of the 15 patients received atypical neuroleptics (mean risperidone equivalent daily dosage = 1.60 mg, SD = 1.31), and the other four received no neuroleptics. The mean illness duration was 4.9 (SD = 4.9) years. Clinical symptoms were assessed by the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham, 1962). The mean score of BPRS was 17.9 (SD = 5.7). The ratings were reviewed by HT and YO after the patient interview, and disagreements were resolved by consensus; consensus ratings were used in this study. Fifteen normal controls (nine men and six women, mean age 29.1 years, SD = 7.8) were recruited from the surrounding community. The candidates were carefully screened and standardized interviews were conducted by trained psychiatrists (HT and YO). They did not meet criteria for any psychiatric disorder. None of the controls were taking alcohol and medication at the time, nor did they have a history of psychiatric disorder, significant physical illness, head injury, neurological disorder, or alcohol or drug dependence. Patients had a tendency of a lower educational status (patients 13.7 ± 1.5 years, controls 14.9 ± 2.4 years; $P = 0.11$, t test). All of the patients and controls were right-handed, and they all underwent an MRI to rule out cerebral anatomic abnormalities. After the procedures had been fully explained to the subjects, written informed consent was obtained, as approved by the Ethics Committee.

Stimulus and self-rating

Stimulus materials were taken from the International Affective Picture System (IAPS) (Lang et al., 1997). Pictures were divided into three emotional classes (neutral, unpleasant, and pleasant) according to the subjective ratings provided by IAPS. We employed 40 pictures from each class. The mean valence and arousal ratings of 40 pictures were 5.87 (SD = 0.77) and 3.75 (SD = 1.11) for neutral, 3.07 (SD = 0.69) and 5.75 (SD = 0.83) for unpleasant, and 7.42 (SD = 0.36) and 4.65 (SD = 0.95) for pleasant pictures. Slides of the three emotional classes were matched for content (faces, human figures, animals, objects, and scenery). The pictures were projected via a computer and a telephoto lens onto a screen with a mirror mounted on a head-coil. The experimental design consisted of eight blocks for each of the three conditions (neutral, unpleasant, and pleasant) interleaved with 20-s rest periods. During the rest condition, subjects viewed a crosshair projected at the center of the screen. In each 20-s block, five different pictures of the same emotional class were presented for 3.5 s each, with an interstimulus interval of 0.5 s. During the scans, the subjects were instructed to indicate how each picture made them feel by categorizing their subjective emotions into three emotional classes (neutral, unpleasant, and pleasant) using buttons. Signals from the buttons were transmitted to a computer outside the shielded room via infrared rays to confirm whether expected emotions were evoked in response to individual affective pictures. The rate of the appearance of expected categorizations from the 40 pictures of the same emotional class was calculated for each emotional condition. We compared the percentages of expected categorizations between the patient and control groups.

fMRI acquisition

The images were acquired with a 1.5-T Signa system (General Electric, Milwaukee, WI). Functional images of 240 volumes were acquired with T2*-weighted gradient echo planar imaging sequences sensitive to blood oxygenation level-dependent (BOLD) contrast. Each volume consisted of 40 transaxial contiguous slices with a slice thickness of 3 mm to cover almost the whole brain (flip angle, 90°; TE, 50 ms; TR, 4 s; matrix, 64 × 64; field of view, 24 × 24).

Analysis of functional imaging data

Data analysis was performed with statistical parametric mapping software package (SPM99) (Wellcome Department of Cognitive Neurology, London, UK) that runs with MATLAB (Mathworks, Natick, MA). All volumes were realigned to the first volume of each session to correct for subject motion and were spatially normalized to the standard space defined by the Montreal Neurological Institute (MNI) template. After normalization, all scans had a resolution of $2 \times 2 \times 2$ mm^3. Functional images were spatially smoothed with a 3D isotropic Gaussian kernel (full width at half maximum of 8 mm). Low frequency noise was removed by applying a high-pass filter (cut-off period = 240 s) to the fMRI time series at each voxel. A temporal smoothing function was applied to the fMRI time series to enhance the temporal signal-to-noise ratio. These images were scaled to give a grand mean signal of 100 across all voxels in all images to remove global effects. Significant hemodynamic changes for each condition were examined using the general linear model with boxcar functions convoluted with a hemodynamic response function. Statistical parametric maps for each contrast of the t statistic were calculated on a voxel-by-voxel basis. The t values were then transformed to unit normal distribution, resulting in z scores.

We assessed the neutral vs. rest, the unpleasant vs. rest, and the pleasant vs. rest contrasts. To assess the specific condition effect, we used the contrasts by subtracting the neutral condition from the pleasant condition and the unpleasant condition. A random effects model, which estimates the error variance for each condition across the subjects, was implemented for group analysis. This procedure provides a better generalization to the population from which data are obtained. The contrast images were obtained from single-subject analysis and were entered into the group analysis. A one-sample *t* test was applied to determine group activation for each effect. Significant clusters of activation were determined using the conjoint expected probability distribution of the height and extent of *z* scores with the height and extent threshold. In addition, we tested for relative differences in the pattern of neural activation by

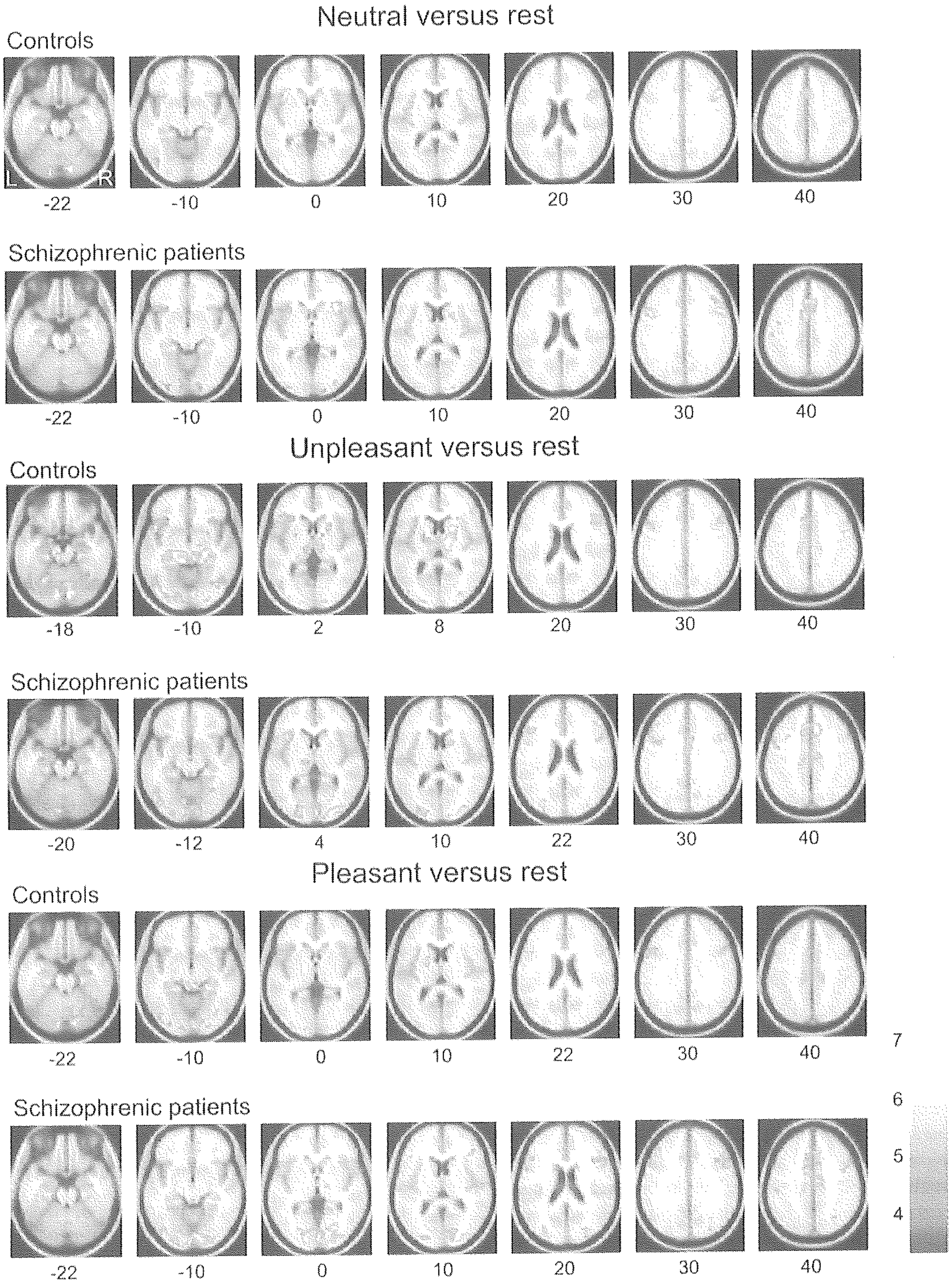


Fig. 1. Images showing brain regions of significant activation during the neutral and unpleasant conditions relative to the rest condition in 15 controls and 15 schizophrenic patients. The bar shows the range of the *z* score. Within the image, L indicates left and R indicates right. Significant differences were accepted at a height threshold ($z > 4.75$; $P < 0.000001$, uncorrected) and extent threshold (30 voxels). Numbers in the bottom row indicate the *z* coordinates of the Montreal Neurological Institute brain.

Table 1
Brain regions of significant activation during unpleasant condition relative to neutral in 15 controls and 15 schizophrenic patients

	Brain region	Brodmann's area	Coordinates[a]			z score[b]
			x	y	z	
Controls	Left lingual gyrus	17, 18, 19	−16	−88	−9	5.61
	Right lingual gyrus	17, 18, 19	8	−82	−1	5.33
	Left fusiform gyrus	19, 37	−32	−76	−8	5.8
	Right fusiform gyrus	18, 37	22	−88	−11	4.95
	Posterior cingulate	31	−2	−53	23	4.39
	Left hippocampal region	34, 35	−18	−26	−12	5.31
	Right hippocampal region	27, 28	24	−24	−9	5.55
	Left amygdala		−24	−3	−18	4.29
	Right amygdala		28	−1	−18	5.02
	Left thalamus		−10	0	7	4.71
	Right thalamus		18	−8	10	4.18
	Left caudate nucleus		−14	10	11	4.7
	Medial .prefrontal cortex	9	−4	50	25	4.73
	Right orbitofrontal cortex	47	32	27	−6	4.65
	Cerebellum		32	−77	−18	6.18
	Midbrain		−6	−33	−8	5.35
Schizophrenia	Left lingual gyrus	17, 18, 19	−18	91	3	4.68
	Right lingual gyrus	17	14	−90	6	4.07
	Left fusiform gyrus	19	−20	−80	−11	4.3
	Right fusiform gyrus	19	24	−80	−11	4.33[c]
	Left amygdala		−22	−6	−18	4.56[c]

[a] Talairach and Tournoux coordinates in the local point of maximal activation included in the cluster.

[b] Significant differences were accepted at a height threshold ($z > 3.89$; $P < 0.00005$, uncorrected) and extent threshold (30 voxels).

[c] Right visual cortex and left amygdala in schizophrenia survived the height threshold but not the extent threshold.

subtracting the unpleasant minus neutral (U − N) contrasts of the patients from the U − N contrasts of the controls and vice versa. Between-group comparison was performed with a two-sample t test. Using the effect sizes, representing the percent signal change, of the U − N contrasts at the regional maxima uncovered in the between-group comparisons, we analyzed whether the BOLD signal change was correlated with the dosage of neuroleptics and the BPRS score. Coordinates of activation were converted from MNI coordinates to Talairach and Tournoux (1988) coordinates using the mni2tal algorithm (M. Brett, Cambridge, MA). Contrast images were overlaid onto a group mean anatomy image provided by SPM for viewing.

Results

Self-rating

The mean percentages of expected categorizations of the controls for the neutral, unpleasant, and pleasant pictures were 85.3% (SD = 8.3), 88.8% (SD = 11.3), and 59.0% (SD = 22.8), respectively, and those of the schizophrenic patients were 81.3% (SD = 8.3), 92.0% (SD = 9.5), and 55.0% (SD = 34.8), respectively. Two-way repeated-measures analysis of variance of the percentages of expected categorizations showed a significant main effect of condition ($F = 27.6$, $df = 2, 84$, $P < 0.001$), but not a significant main effect of group ($F = 0.26$, $df = 1, 84$, $P = 0.61$) or interaction ($F = 0.44$, $df = 2, 84$, $P = 0.64$). A post hoc test revealed that the percentage of expected category for the pleasant pictures was lower than those for the neutral and unpleasant pictures. That is, the subjects did not categorize the pleasant pictures as we had expected. Most of the remaining pictures not regarded as pleasant were categorized as neutral.

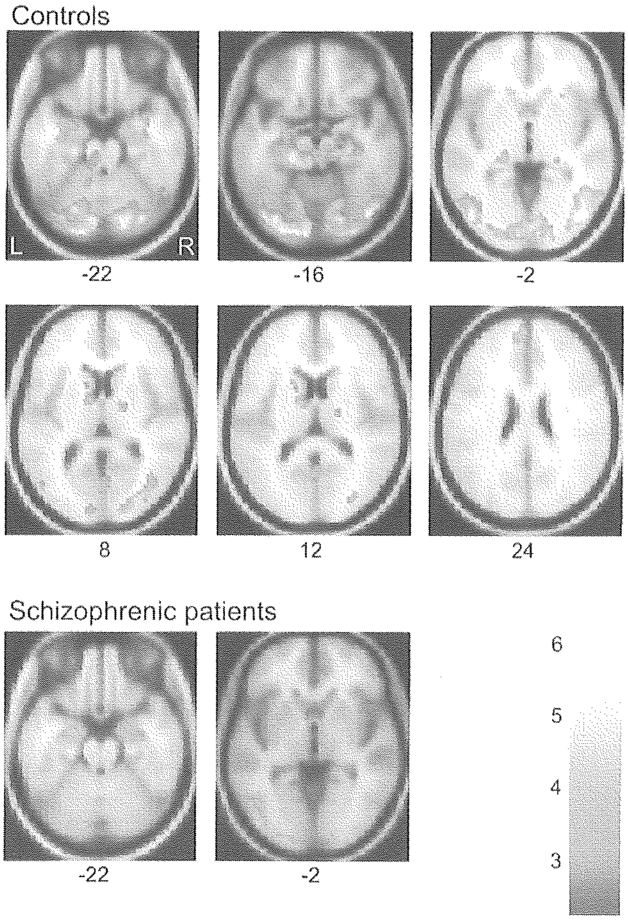


Fig. 2. Images showing brain regions of significant activation during unpleasant condition relative to neutral in 15 controls and 15 schizophrenic patients. The bar shows the range of the z score. Within the image, L indicates left and R indicates right. Significant differences were accepted at a height threshold ($z > 3.89$; $P < 0.00005$, uncorrected) and extent threshold (30 voxels). (Right visual cortex and left amygdala in the schizophrenic patients survived the height threshold but not the extent threshold.) Numbers in the bottom row indicate the z coordinates of the Montreal Neurological Institute brain.